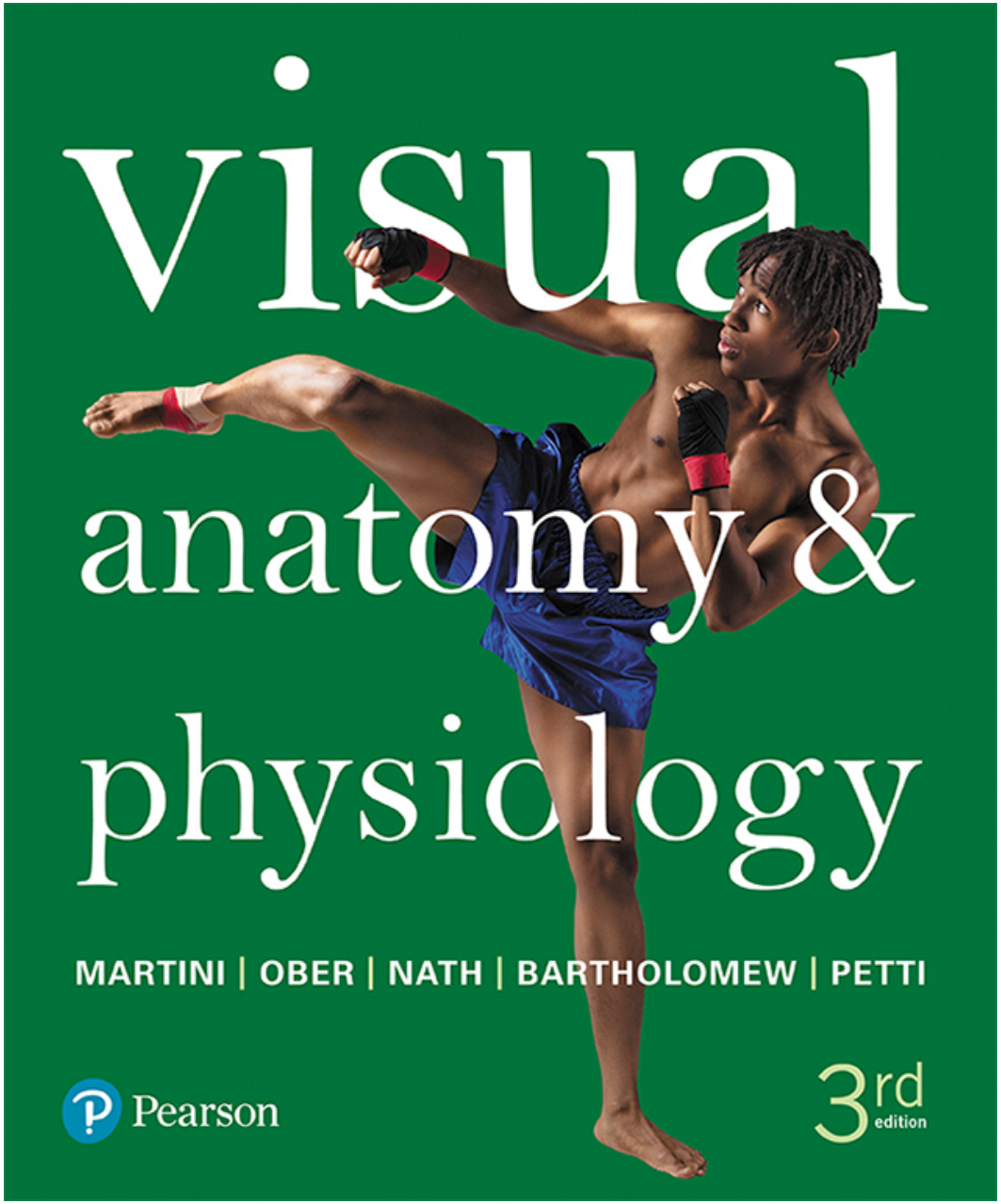

20

The Lymphatic System and Immunity

Lecture Presentation by
Lori Garrett

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Section 1: Anatomy of the Lymphatic System

Learning Outcomes

20.1 Identify the various components of the lymphatic system.

20.2 Describe the structure and function of important lymphatic vessels.

20.3 Describe the lymph-collecting vessels, and explain lymphedema.

20.4 Identify the classes of lymphocytes, discuss their importance, and describe their distribution in the body.

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Section 1: Anatomy of the Lymphatic System

Learning Outcomes (continued)

20.5 Describe lymphoid tissues, and trace lymph flow through a lymph node.

20.6 Describe the structure and function of the thymus.

20.7 Describe the structure and function of the spleen, and trace blood flow through it.

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Module 20.1: The lymphatic system consists of lymphatic vessels, nodes, and lymphoid tissue

Lymphatic system

- Includes cells, tissues, and organs responsible for two functions
  1. **Immunity**
     - Ability to resist infection and disease
     - All cells and tissues involved in immunity are part of the **immune system**
  2. Maintaining normal blood volume and composition of interstitial fluid

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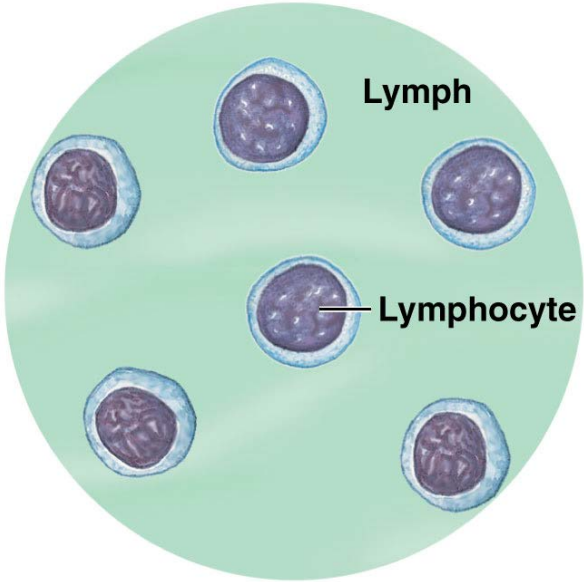
Module 20.1: Lymphatic system overview

Lymphatic system components



- **Lymphocytes**
  - Primary cells of the lymphatic system
  - Respond to:
    - Invading pathogens (such as bacteria and viruses)
    - Abnormal body cells (such as virus-infected or cancer cells)
    - Foreign proteins (such as bacterial toxins)
  - Surrounded by **lymph**
    - Interstitial fluid that has entered a lymphatic vessel

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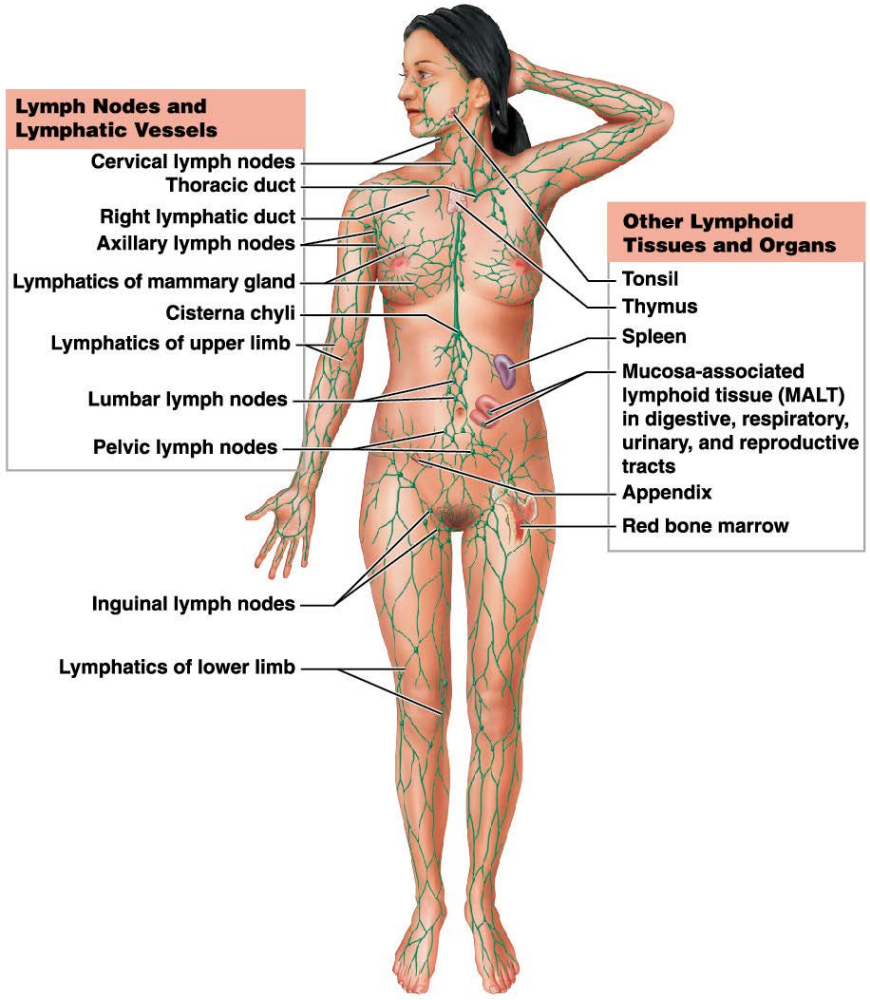
Module 20.1: Lymphatic system overview

Lymphatic system components (continued)

- **Lymphatic vessels**
  - Often called **lymphatics**
  - Begin in peripheral tissues
  - End at connections to veins



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Module 20.1: Lymphatic system overview

Lymphatic system components (continued)

- Lymphoid tissues and lymphoid organs
  - Scattered throughout the body
  - **Primary lymphoid tissues and organs**
    - Sites where lymphocytes are formed or mature
    - Include red bone marrow and the thymus gland
  - **Secondary lymphoid tissues and organs**
    - Where lymphocytes are activated and cloned (copied)
    - Include lymph nodes, tonsils, MALT, appendix, and spleen

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Module 20.1: Review

A. What is the difference between a lymphocyte and lymph?
B. List the components of the lymphatic system.

Learning Outcome: Identify the various components of the lymphatic system.

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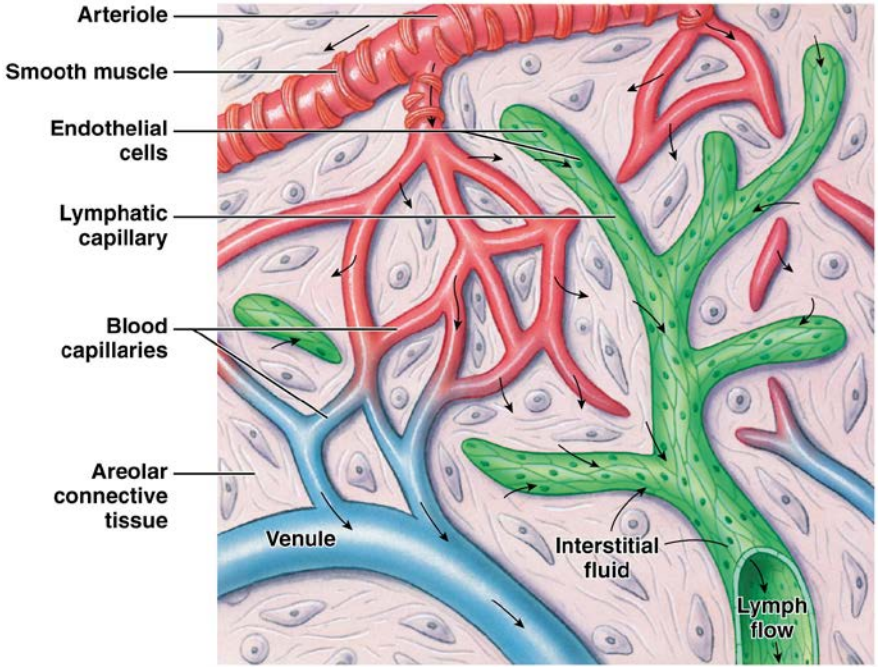
Module 20.2: Interstitial fluid flows continuously into lymphatic capillaries and exits tissues as lymph in lymphatic vessels

Lymphatic vessels

- Carry lymph from peripheral tissues to venous system
- Found in close association with blood vessels
- Network begins with **lymphatic capillaries** (smallest vessels)



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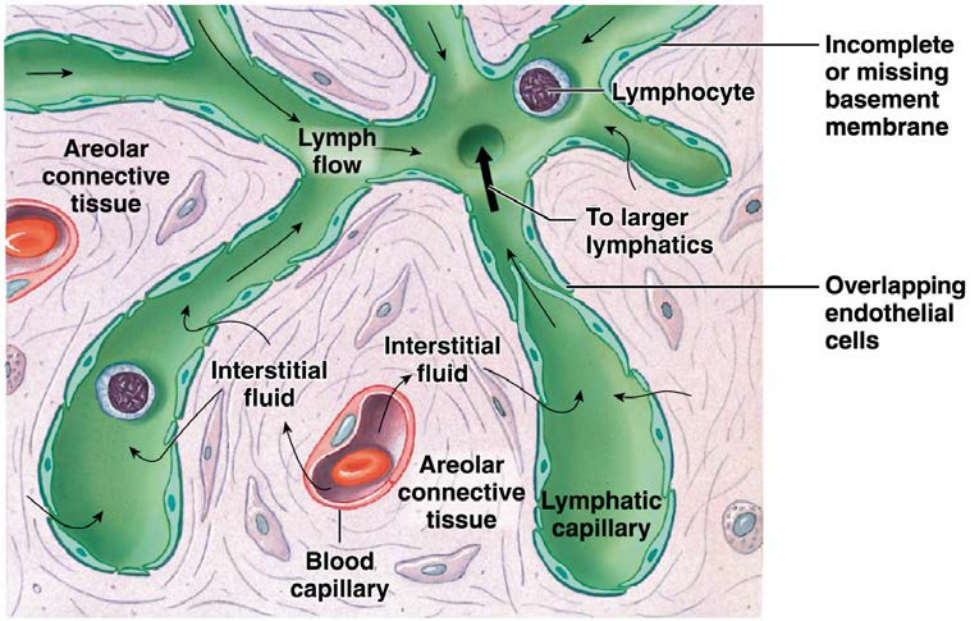
Module 20.2: Lymphatic vessels

Lymphatic capillaries

- Differ from blood capillaries
  - Closed at one end
  - Have larger diameters
  - Have thinner walls
    - Basement membrane is incomplete or absent
  - Typically have a flattened or irregular outline in sectional view



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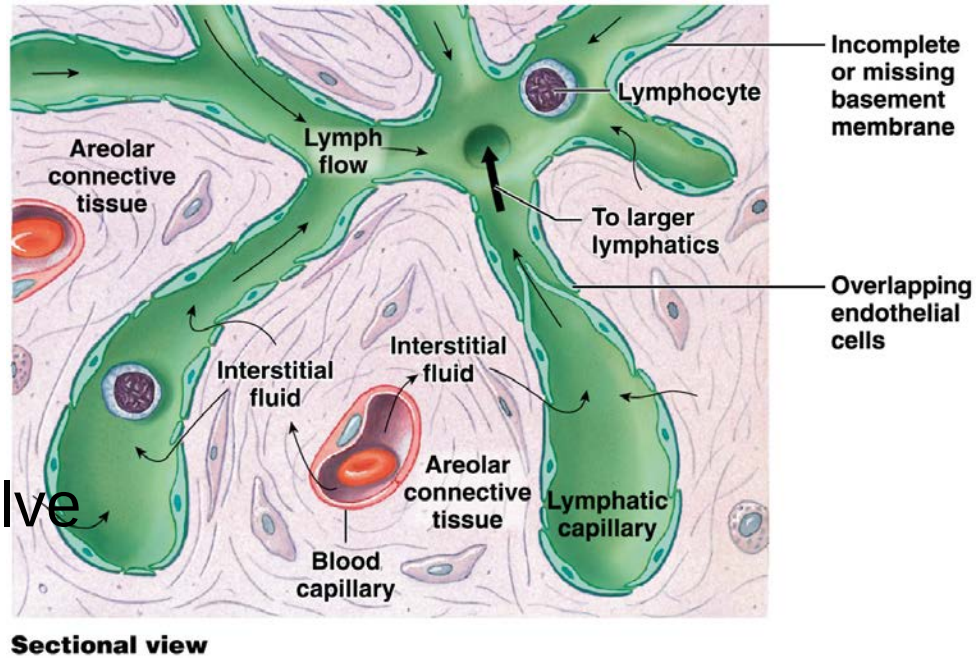
Module 20.2: Lymphatic vessels

Lymphatic capillaries (continued)

- Have overlapping endothelial cells
  - Region of overlap acts as a one-way valve
  - Permits entry of fluid and solutes (including proteins)
    - Also allows entry of viruses, bacteria, cell debris
  - Prevents return of these materials to the intercellular space



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Module 20.2: Lymphatic vessels

Lymphatic vessel structure

- Lymph flows into larger lymphatic vessels that lead toward the body's trunk
- Small to medium-sized lymphatic vessels contain valves
  - Valves located close together
  - Vessel bulges at each valve
    - Series of bulges makes vessel resemble string of pearls
  - Low pressure in lymphatic vessels
  - Valves prevent backflow of lymph
  - Contraction of surrounding skeletal muscles aids flow of lymph

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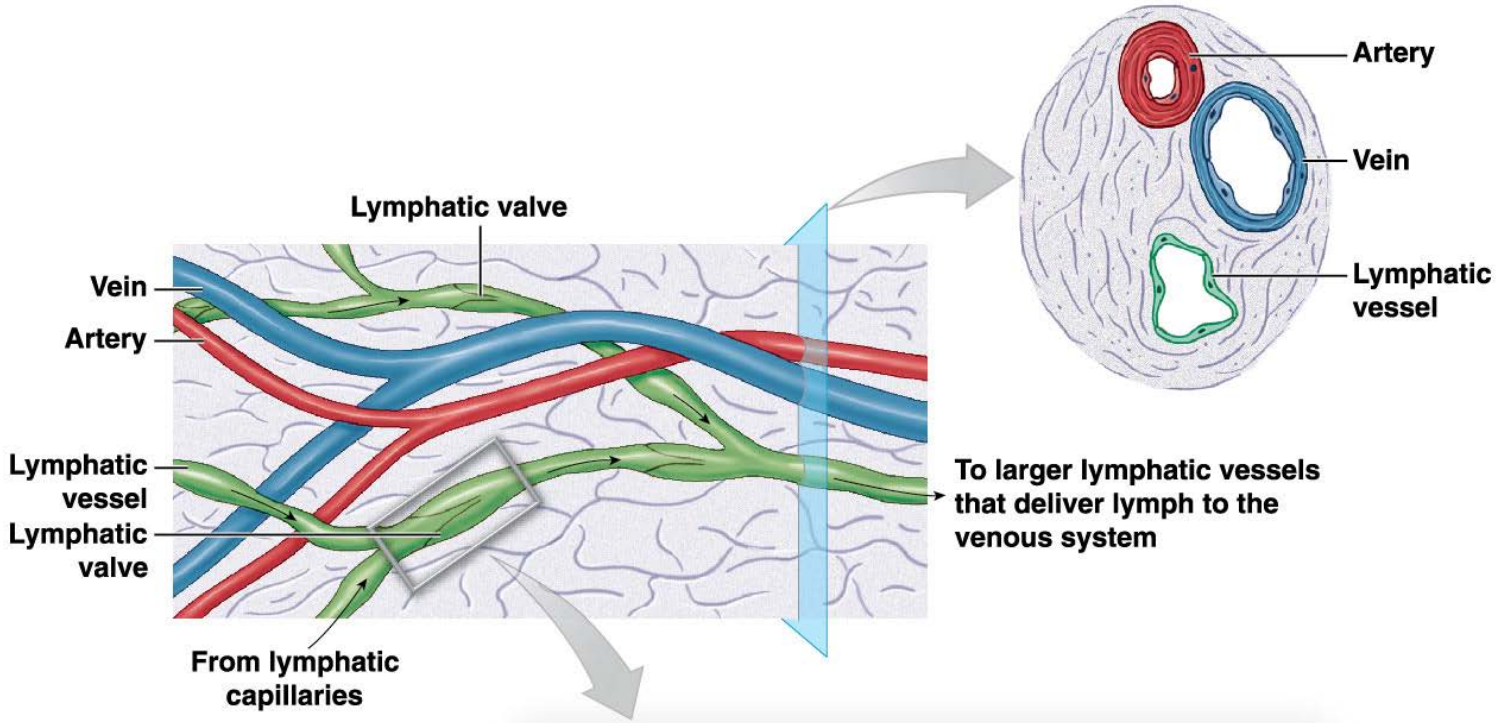
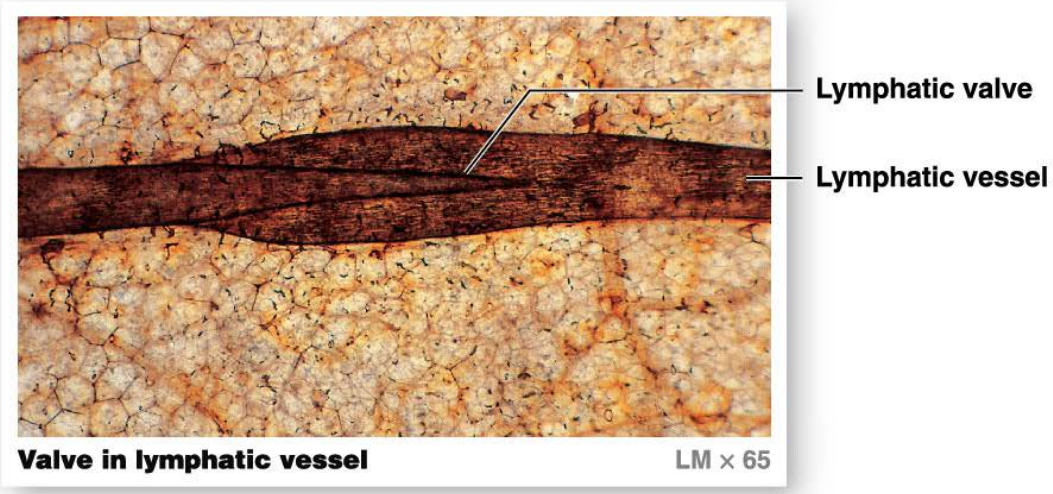
Lymphatic vessels





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Module 20.2: Lymphatic vessels

Distribution of lymphatic vessels

- In the small intestine
  - Prominent lymphatic capillaries called *lacteals*
  - Important in the transport of lipids absorbed from the digestive tract
- Areas lacking lymphatic capillaries
  - Areas without a blood supply
    - *Example:* cornea of eye

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Module 20.2: Review

A. What is the function of lymphatic vessels?
B. What is the function of overlapping endothelial cells in lymphatic capillaries?
C. What structure prevents the backflow of lymph in some lymphatic vessels?
D. Compare lymphatic capillaries in the small intestine with those found elsewhere.

Learning Outcome: Describe the structure and function of important lymphatic vessels.

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Module 20.3: Small lymphatic vessels converge to form lymphatic ducts that empty into the subclavian veins

Lymphatic vessel locations

- **Superficial lymphatics**
  - Subcutaneous layer deep to skin
  - Areolar tissues of mucous membranes (digestive, respiratory, urinary, and reproductive tracts)
  - Areolar tissues of serous membranes (pleural, pericardial, and peritoneal cavities)
- **Deep lymphatics**
  - Accompany deep arteries and veins supplying skeletal muscles and other organs of the neck, limbs, and trunk, and wall of visceral organs

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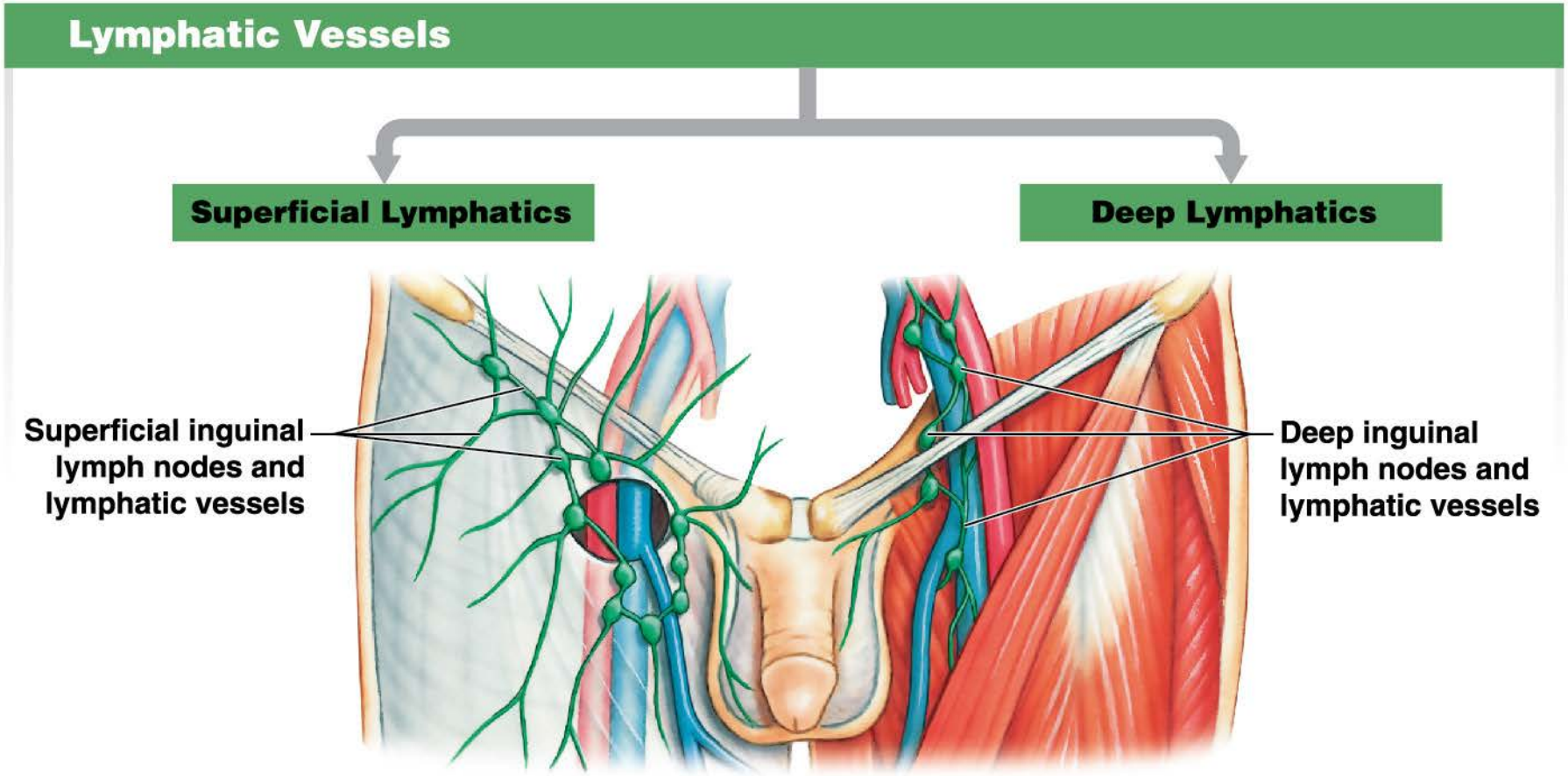
Superficial and deep lymphatics



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Module 20.3: Lymphatic flow

Collecting vessels

- Superficial and deep lymphatics converge to form **lymphatic trunks**, which empty into:
  1. **Thoracic duct**
     - Collects lymph from:
       - Entire body inferior to the diaphragm
       - The left side of the body superior to the diaphragm
     - Drains into the left subclavian vein
  2. **Right lymphatic duct**
     - Collects lymph from:
       - The right side of the body superior to the diaphragm
     - Drains into the right subclavian vein

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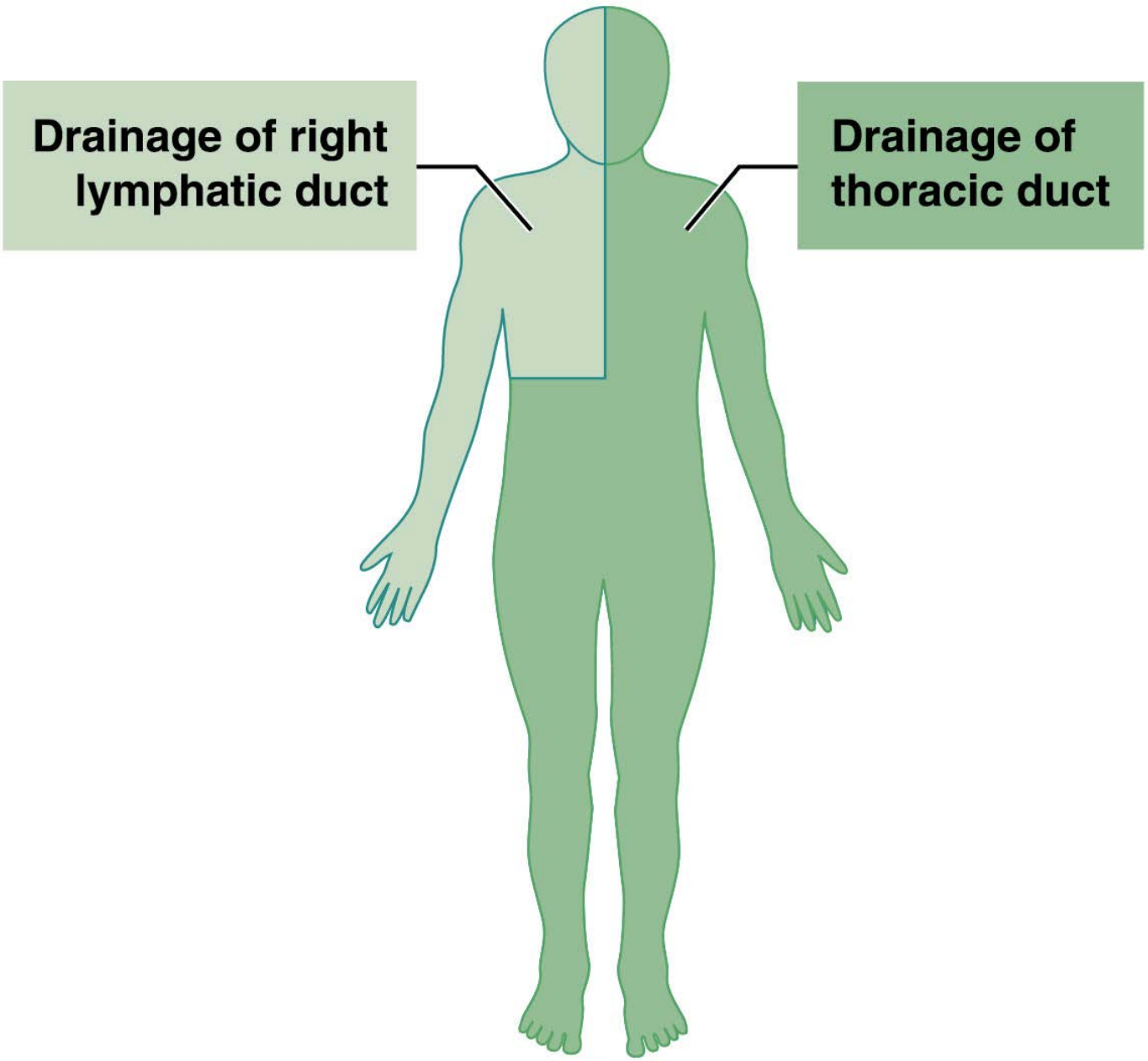
Collecting vessels



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Module 20.3: Lymphatic flow

Right lymphatic duct

- Formed by merging of the:
  - **Right jugular trunk**
  - **Right subclavian trunk**
  - **Right bronchomediastinal trunk**

Thoracic duct

- Collects lymph from:
  - **Left bronchomediastinal trunk**
  - **Left subclavian trunk**
  - **Left jugular trunk**

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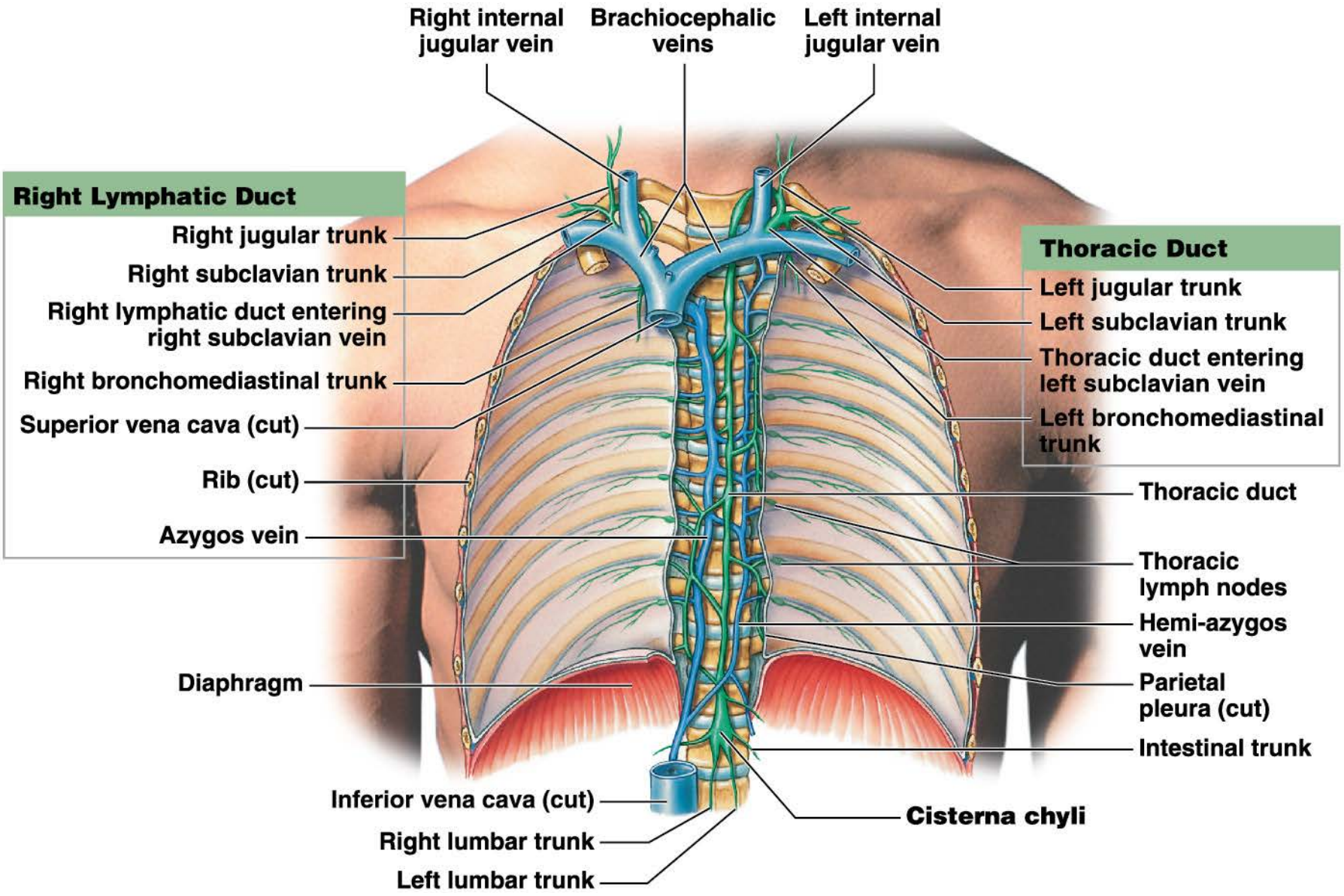
Right lymphatic duct and thoracic duct



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Module 20.3: Lymphatic flow

Cisterna chyli

- Expanded, sac-like chamber at the base of the thoracic duct
  - Receives lymph from:
    - The inferior part of the abdomen
    - The pelvis
    - The lower limbs
  - Lymph is drained into the cysterna chyli by the:
    - **Lumbar trunks**
    - **Intestinal trunk**

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Module 20.3: Lymphatic flow

Lymphedema

- Caused by blocked lymphatic drainage
  - Interstitial fluids accumulate
  - Affected area becomes swollen and distended
- Most often seen in limbs but can affect other areas
- Swelling may become permanent
  - Connective tissue loses elasticity
- Stagnant interstitial fluids may accumulate toxins and pathogens
  - Local immune defenses overwhelmed

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Module 20.3: Review

A. Describe the drainage of the right lymphatic duct and the thoracic duct.
B. Name the two large lymphatic vessels into which the lymphatic trunks empty.
C. Explain lymphedema.

Learning Outcome: Describe the lymph-collecting vessels, and explain lymphedema.

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Module 20.4: Lymphocytes are responsible for the immune functions of the lymphatic system

Lymphocytes

- Make up 20–40 percent of circulating leukocytes
- Most lymphocytes are out in lymphatic tissues
- Three classes circulate in blood
  1. **T cells** (~80 percent of circulating lymphocytes)
     - **Cell-mediated immunity**
  2. **B cells** (10–15 percent of circulating lymphocytes)
     - **Antibody-mediated immunity**
  3. **NK cells** (5–10 percent of circulating lymphocytes)
     - **Immune surveillance**

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Module 20.4: Lymphocytes

Lymphocytes (continued)

- All classes of lymphocytes are sensitive to specific chemicals (**antigens**)
  - Most antigens are pathogens, foreign proteins, or abnormal substances
  - Antigens stimulate an *immune response*
    - Leads to destruction of the target compound or organism

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Module 20.4: Lymphocytes

Lymphocyte classes

- **T cells**
  1. **Cytotoxic T cells**
     - Attack foreign cells or body cells infected by viruses
     - Attack commonly involves direct contact
     - Primary cells involved in production of **cell-mediated immunity** (cellular immunity)
  2. **Helper T cells**
     - Stimulate activation and function of T cells and B cells
     - Activate B cells before B cells can produce antibodies

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Module 20.4: Lymphocytes

Lymphocyte classes (continued)

- **T cells** (continued)
  3. **Regulatory T cells**
     - Moderate immune response
     - Helps establish and control sensitivity of immune response
  4. **Memory T cells**
     - Respond to antigens they have already encountered

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Module 20.4: Lymphocytes

Lymphocyte classes (continued)

- **B cells**
  - When stimulated, become **plasma cells** that produce and secrete antibodies
  - Responsible for **antibody-mediated immunity** (humoral immunity)
    - Antibodies circulate in body fluids to attack targets throughout the body

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Module 20.4: Lymphocytes

Lymphocyte classes (continued)

- **NK** (**natural killer**) **cells**
  - Attack foreign cells, virus-infected body cells, and cancer cells
  - Provide continuous monitoring of peripheral tissues
    - **Immune surveillance**

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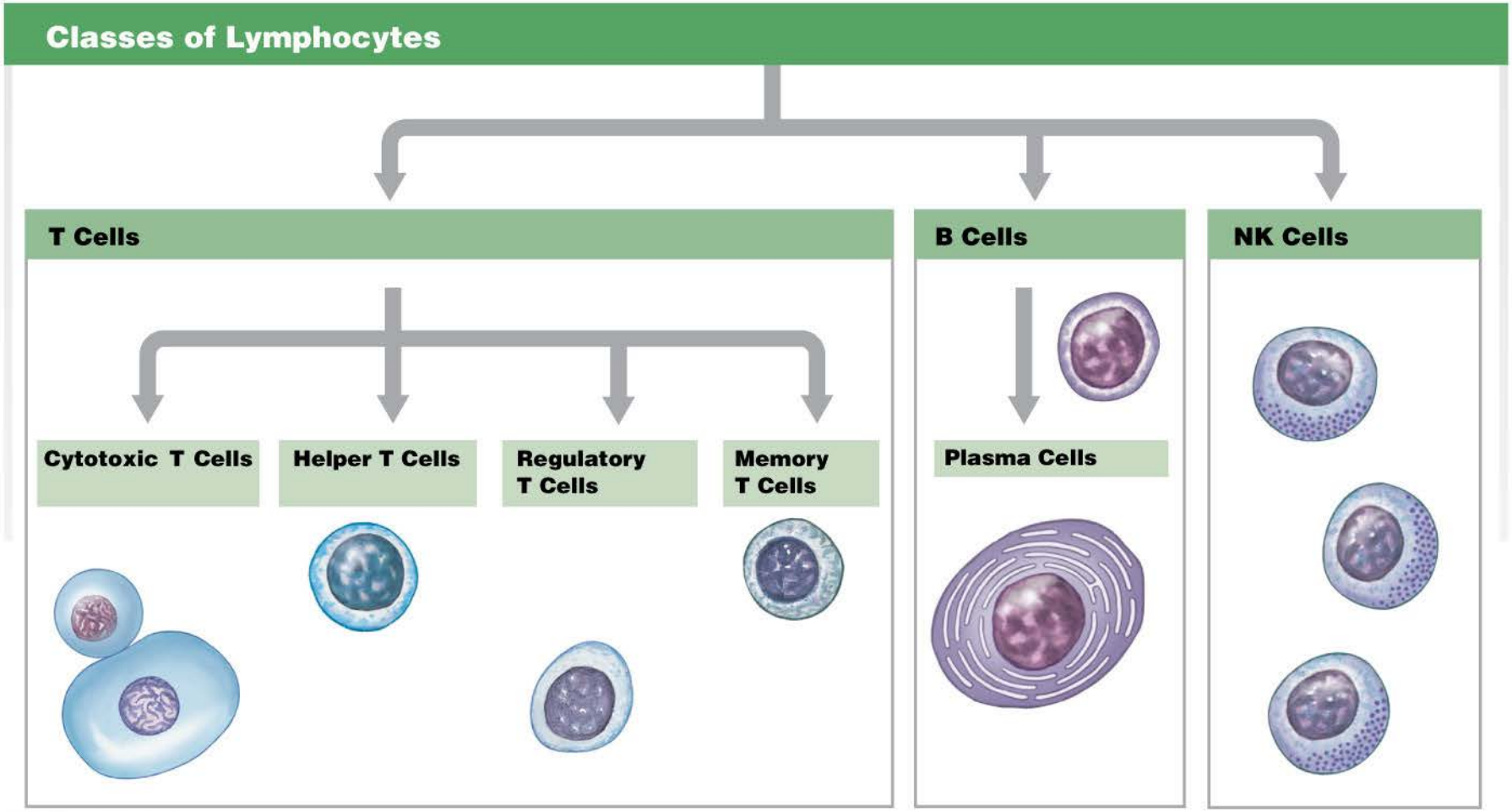
Types of lymphocytes



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Module 20.4: Lymphocytes

Lymphopoiesis (**lymphocyte production**)

- Involves:
  - Red bone marrow
  - Thymus
  - Peripheral lymphoid tissues
- Red bone marrow plays the primary role in maintaining the normal lymphocyte population
  - Hematopoietic stem cells here produce **lymphoid stem cells**

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Module 20.4: Lymphocytes

Lymphopoiesis (continued)

- **Lymphoid stem cells**
  - Produce all lymphocyte types from two groups
    1. One group migrates to the thymus and will develop into T cells
    2. Second group stays in the red bone marrow and divides to produce:
       - B cells
         - Mature and move into lymph nodes, spleen, and other lymphoid tissue
       - NK cells
         - Mature and migrate throughout the body, patrolling peripheral tissues

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Module 20.4: Lymphocytes

Lymphopoiesis (continued)

- Development of stem cells in the thymus
  - Isolated from general circulation by the *blood thymus barrier*
  - Divide in response to thymic hormones to produce all types of T cells
  - T cells undergo selection process
    - Ensuring they won't react to normal body cells
    - Up to 98 percent of T cells are deselected and die
  - Mature T cells re-enter bloodstream
    - Travel to peripheral lymphoid tissues and organs

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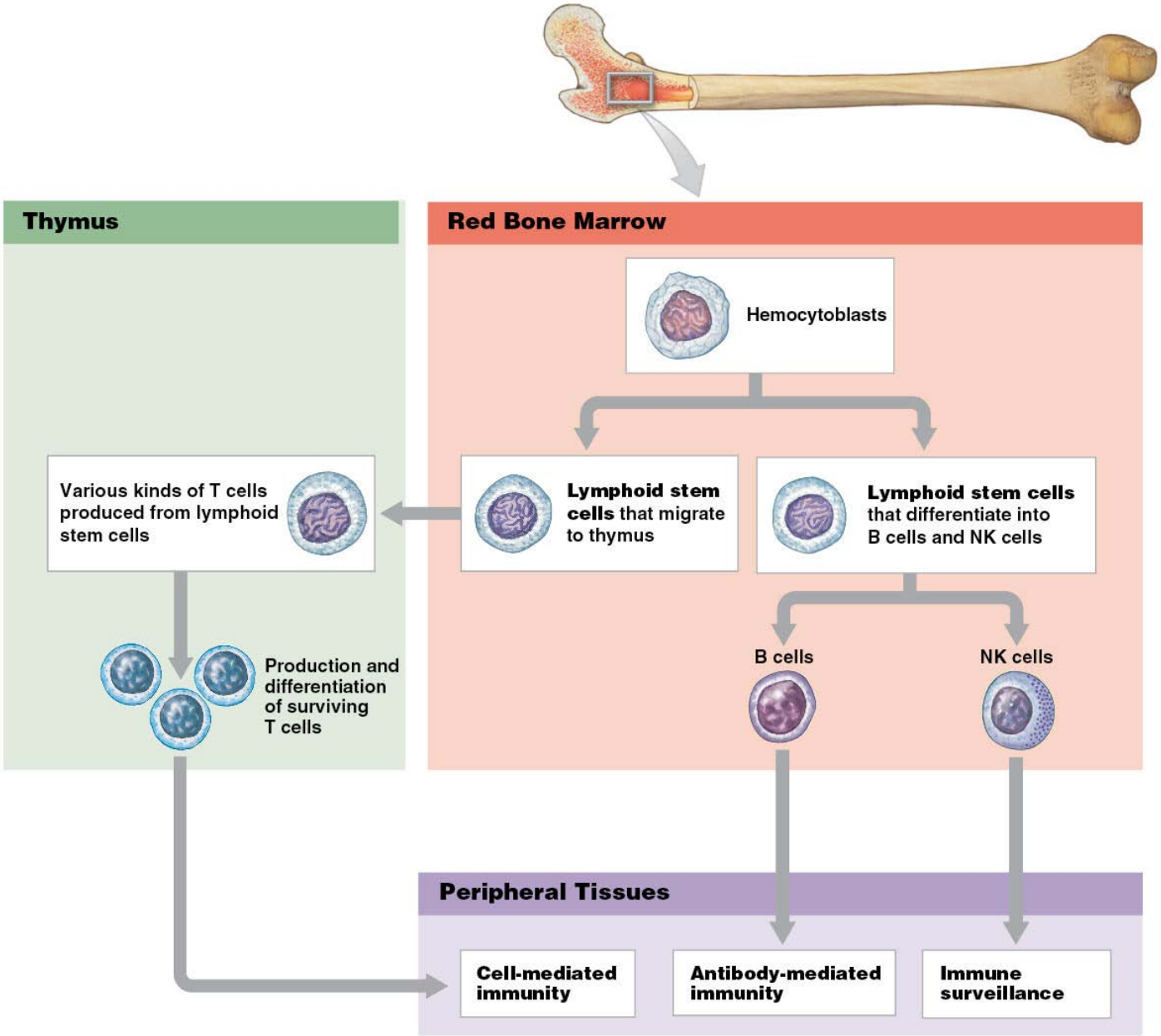
Lymphocytopoiesis



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Module 20.4: Lymphocytes

Lymphopoiesis (continued)

- T cells and B cells
  - Migrate from their sites of origin
  - Retain their ability to divide
    - Producing daughter cells of the same type
    - *Example:* B cell produces more B cells
  - Ability to increase in number is crucial to a successful immune response

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Module 20.4: Review

A. Identify the three main classes of lymphocytes.
B. What tissues are involved in lymphopoiesis?
C. Which cells are responsible for antibody-mediated immunity?

Learning Outcome: Identify the classes of lymphocytes, discuss their importance, and describe their distribution in the body.

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Module 20.5: Lymphocytes aggregate within lymphoid tissues and lymphoid organs

Lymphoid tissues

- Connective tissues dominated by lymphocytes
- **Lymphoid nodules**
  - Densely packed lymphocytes in an area of areolar tissue
  - Nodules may cluster together and form larger masses
  - No fibrous capsule surrounds the masses
- **Lymphoid organs**
  - Separated from surrounding tissues by fibrous connective tissue capsule

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Module 20.5: Lymphoid tissues and organs

Lymphoid nodule locations

- **Aggregated lymphoid nodules** (Peyer's patches)
  - Clusters of lymphoid nodules deep to the epithelial lining of the intestines
  - Each nodule often has a central zone (**germinal center**) containing dividing lymphocytes

Aggregated lymphoid nodules LM × 20

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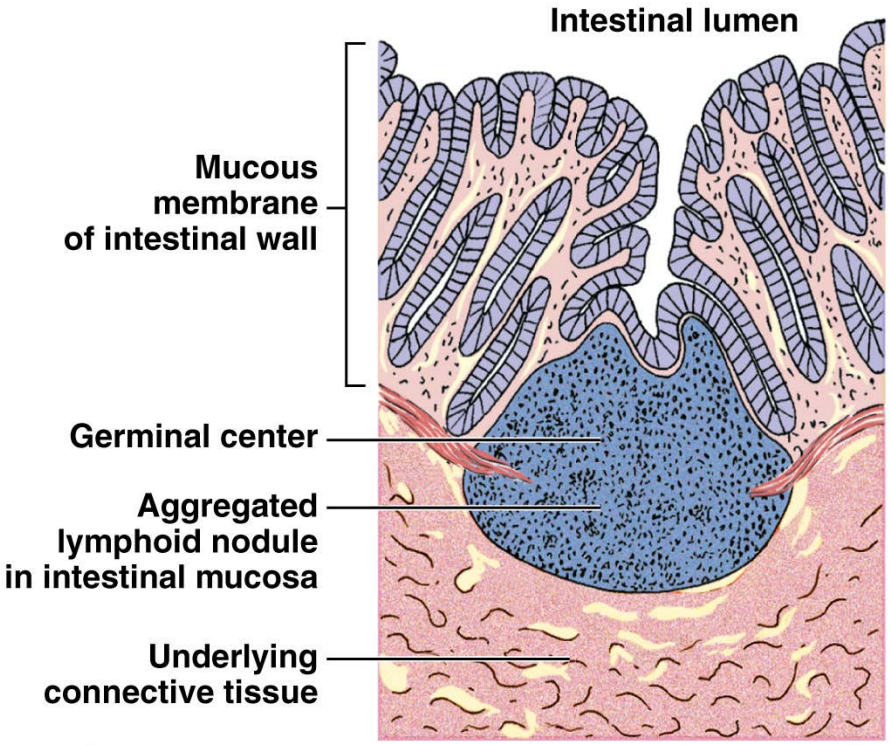
Module 20.5: Lymphoid tissues and organs

Lymphoid nodule locations (continued)

- **Mucosa-associated lymphoid tissue** (**MALT**)
  - Protect epithelia of digestive, respiratory, urinary, and reproductive tracts from pathogens and toxins



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Module 20.5: Lymphoid tissues and organs

Tonsils

- Large lymphoid nodules in the walls of the pharynx
  - **Pharyngeal tonsil** (or the *adenoid*)
    - Located on posterior superior wall of the nasopharynx
  - **Palatine tonsils** (left and right)
    - Located at posterior, inferior margin of the oral cavity along the boundary of the pharynx
  - **Lingual tonsils**
    - Pair of tonsils located deep to the epithelium covering the base of the tongue
- **Tonsillitis**—inflammation of tonsils

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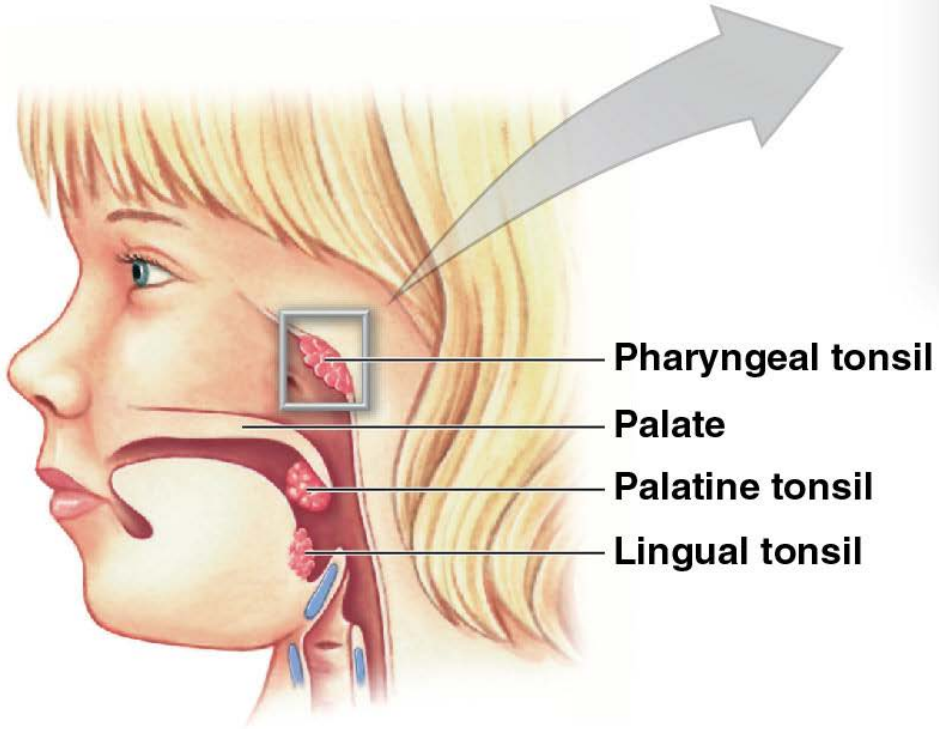
Tonsils



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Module 20.5: Lymphoid tissues and organs

Lymph nodes

- Small lymphoid organs surrounded by fibrous connective tissue capsule
  - Shape resembles a kidney bean
- Diameter range 1–25 mm (about 1 in.)
- Large lymph nodes (**lymph glands**) located in neck, groin, axillae
- Function as filters, removing 99 percent of pathogens from lymph before fluid returns to bloodstream
- **Trabeculae**—fibrous partitions extending inward from capsule

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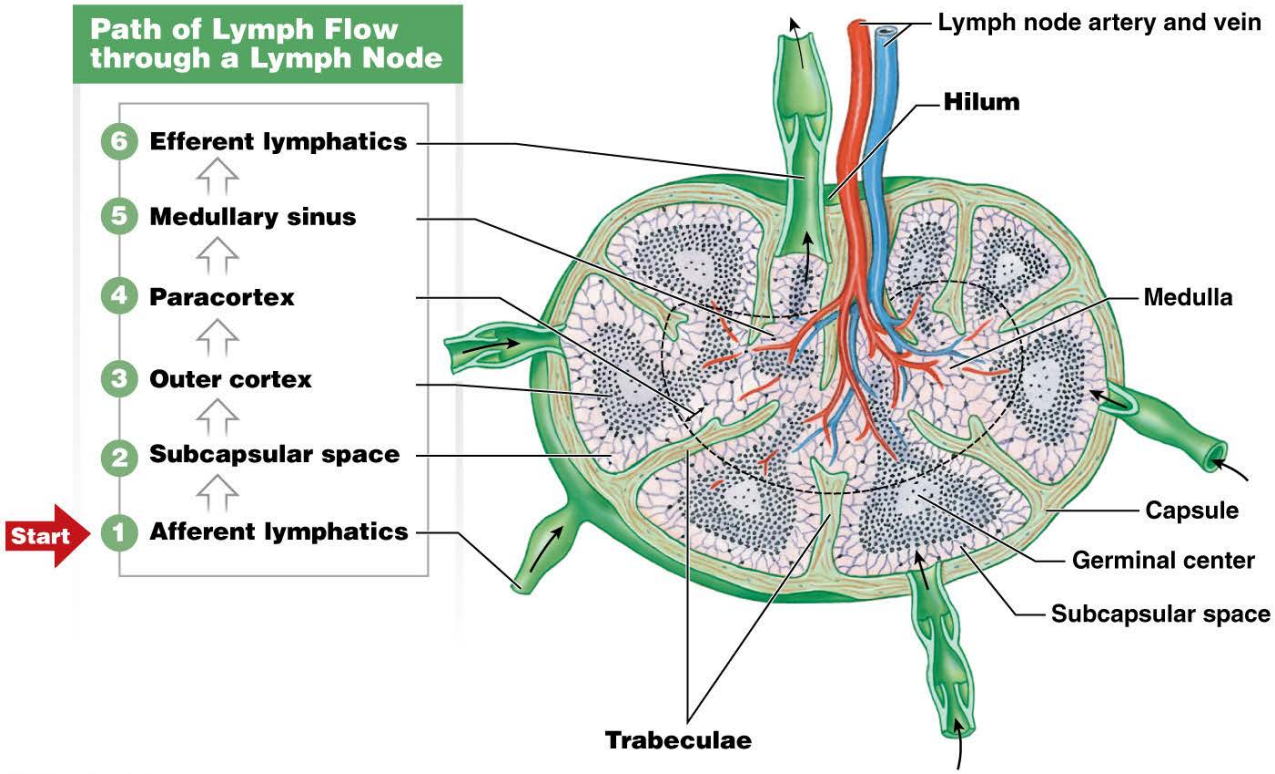
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node

1. **Afferent** (*afferens*, to bring to) **lymphatics** bring lymph into the node on the opposite side from the **hilum** (indentation)



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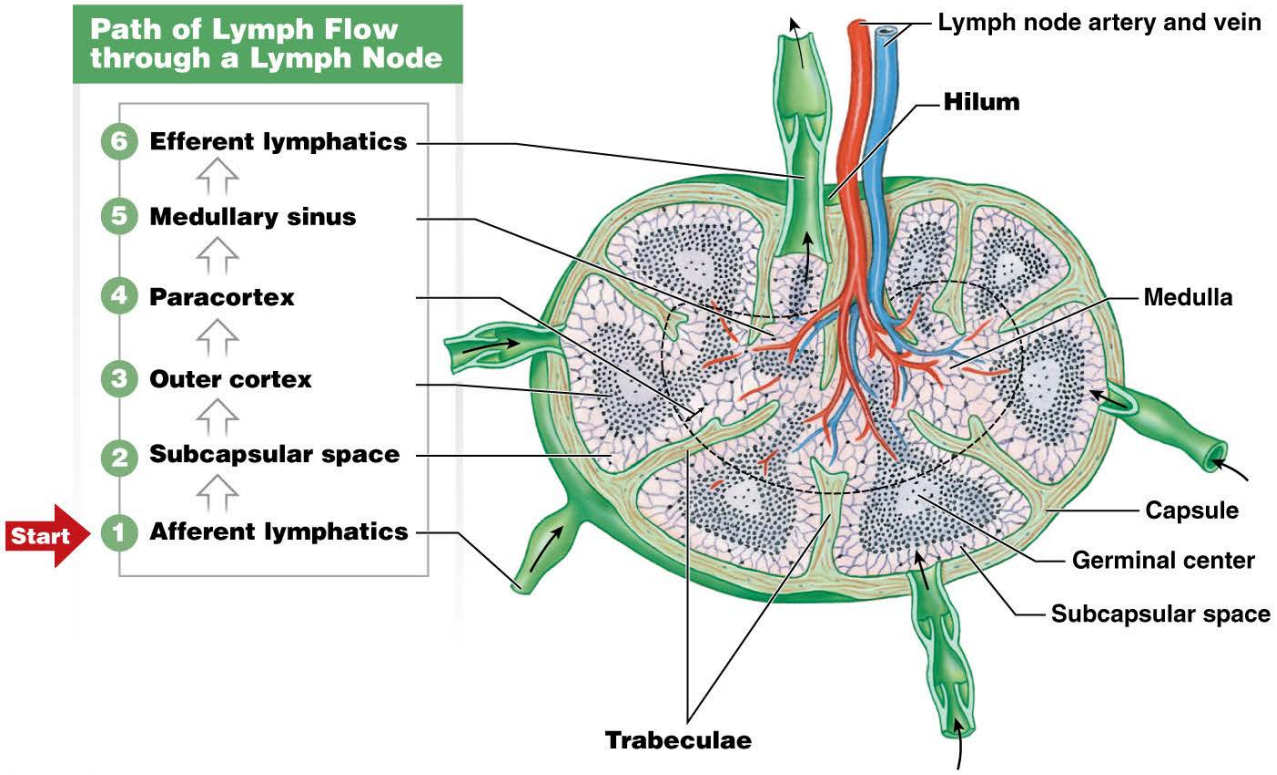
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node (continued)

2. Through the subcapsular space
   - Network of fibers and **dendritic cells** (involved in immune response)



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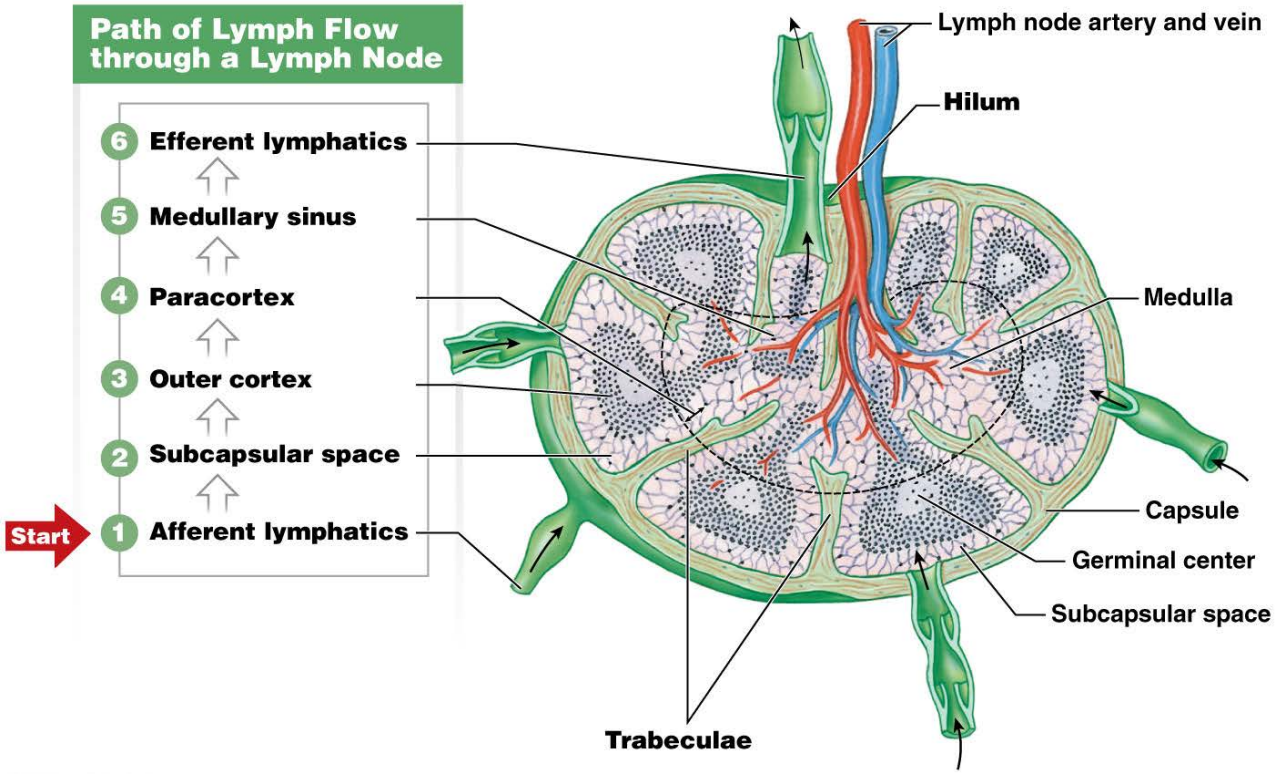
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node (continued)

3. Into the **outer cortex**
   - Contains B cells within germinal centers



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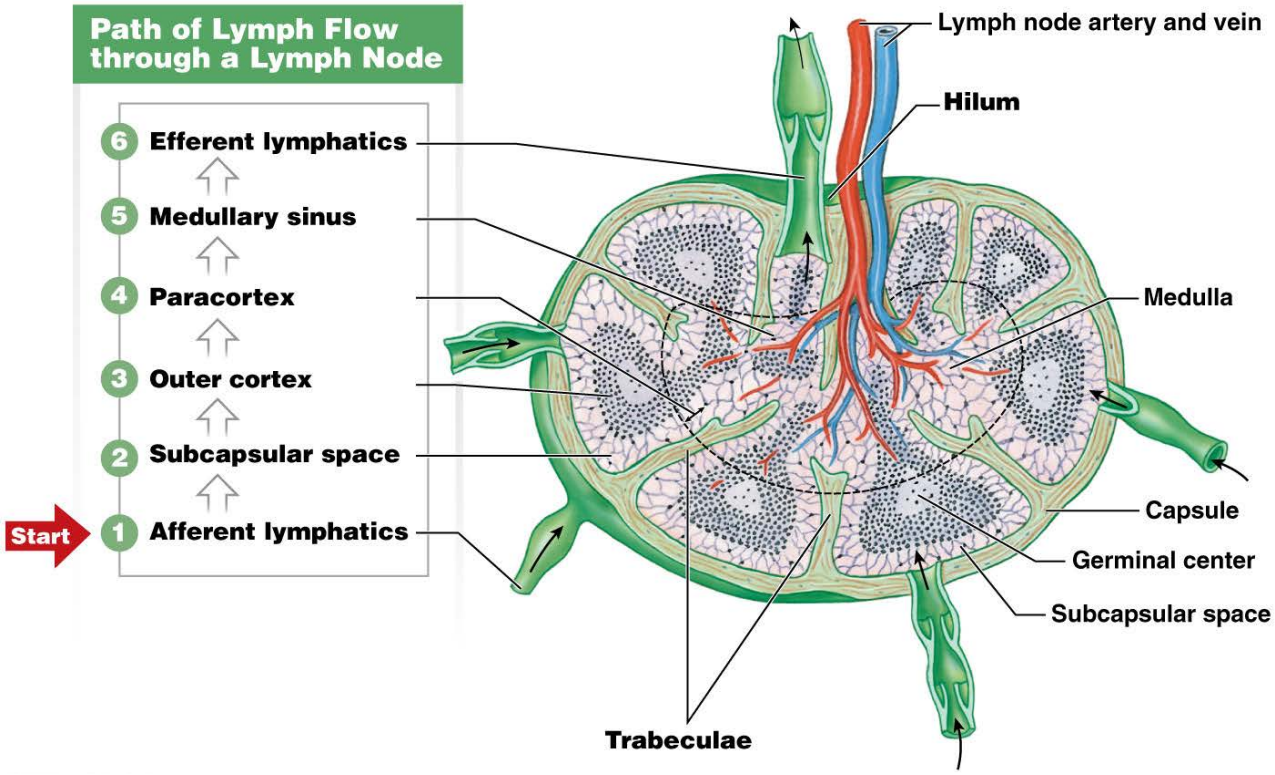
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node (continued)

4. Through lymph sinuses in the **paracortex**
   - Contains T cells



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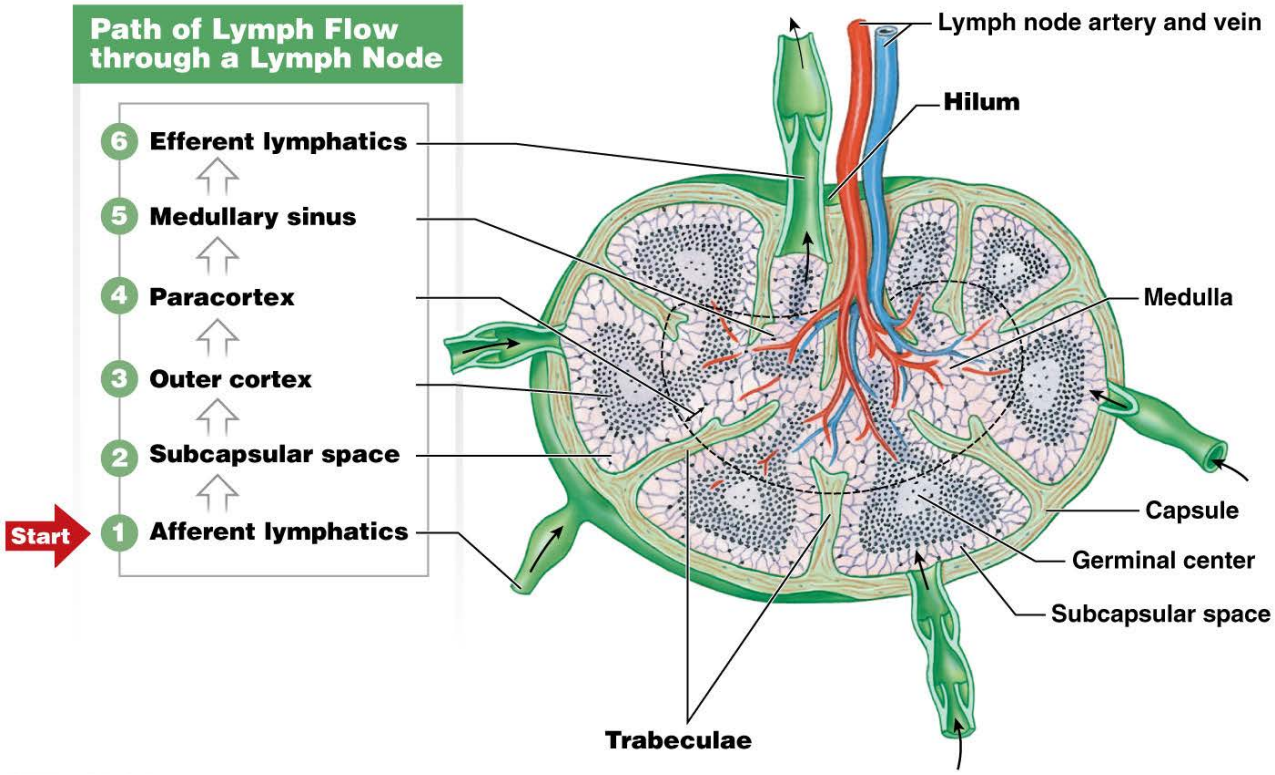
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node (continued)

5. Into the **medullary sinus** at the core
   - Contains B cells and plasma cells



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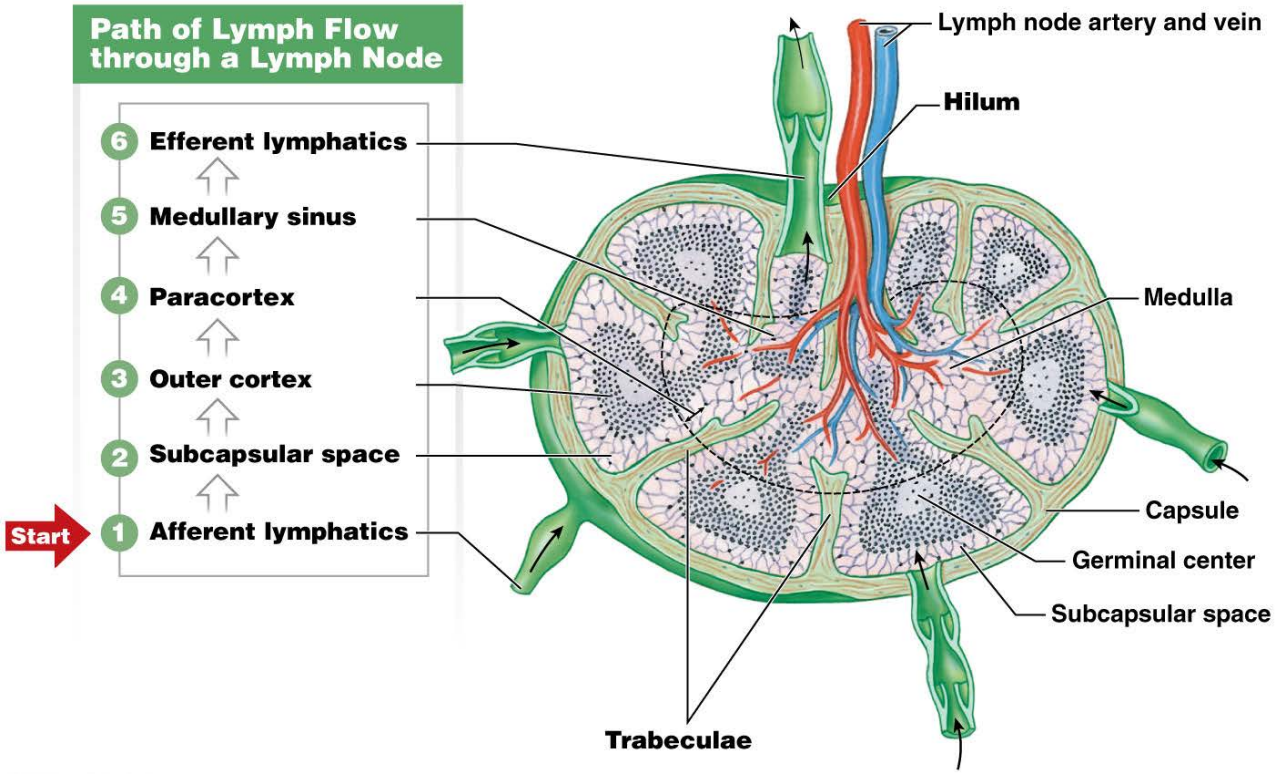
Module 20.5: Lymphoid tissues and organs

Path of lymph through a lymph node (continued)

6. Out of the lymph node in **efferent** (*efferens*, to bring out) **lymphatics** at the hilum and into venous circulation



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Module 20.5: Lymphoid tissues and organs

Clinical disorders

- MALT defends exposed epithelia in multiple tracts exposed to the exterior environment
- Infection and/or inflammation of MALT components can cause variety of clinical disorders
  - *Examples:*
    - **Tonsillitis** (inflammation of the tonsils)
    - **Appendicitis** (inflammation of the lymphoid tissue in the appendix)

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Module 20.5: Review

A. Name the lymphoid tissue that protects epithelia lining the digestive, respiratory, urinary, and reproductive tracts.
B. Define *tonsil*, and name the five tonsils.
C. Trace the path of lymph through a lymph node, beginning at the afferent lymphatics.

Learning Outcome: Describe lymphoid tissues, and trace lymph flow through a lymph node.

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Module 20.6: The thymus is a lymphoid organ that produces functional T cells

Thymus size and function

- Produces several hormones (**thymosins**) important in functional T cell development
- Size and secretory abilities decline with age
  - Size is largest (40 g) before puberty
  - Diminishes in size and becomes increasingly fibrous (**involution**)
  - By age 50, size can be <12 g
  - Correlated with increased susceptibility to disease

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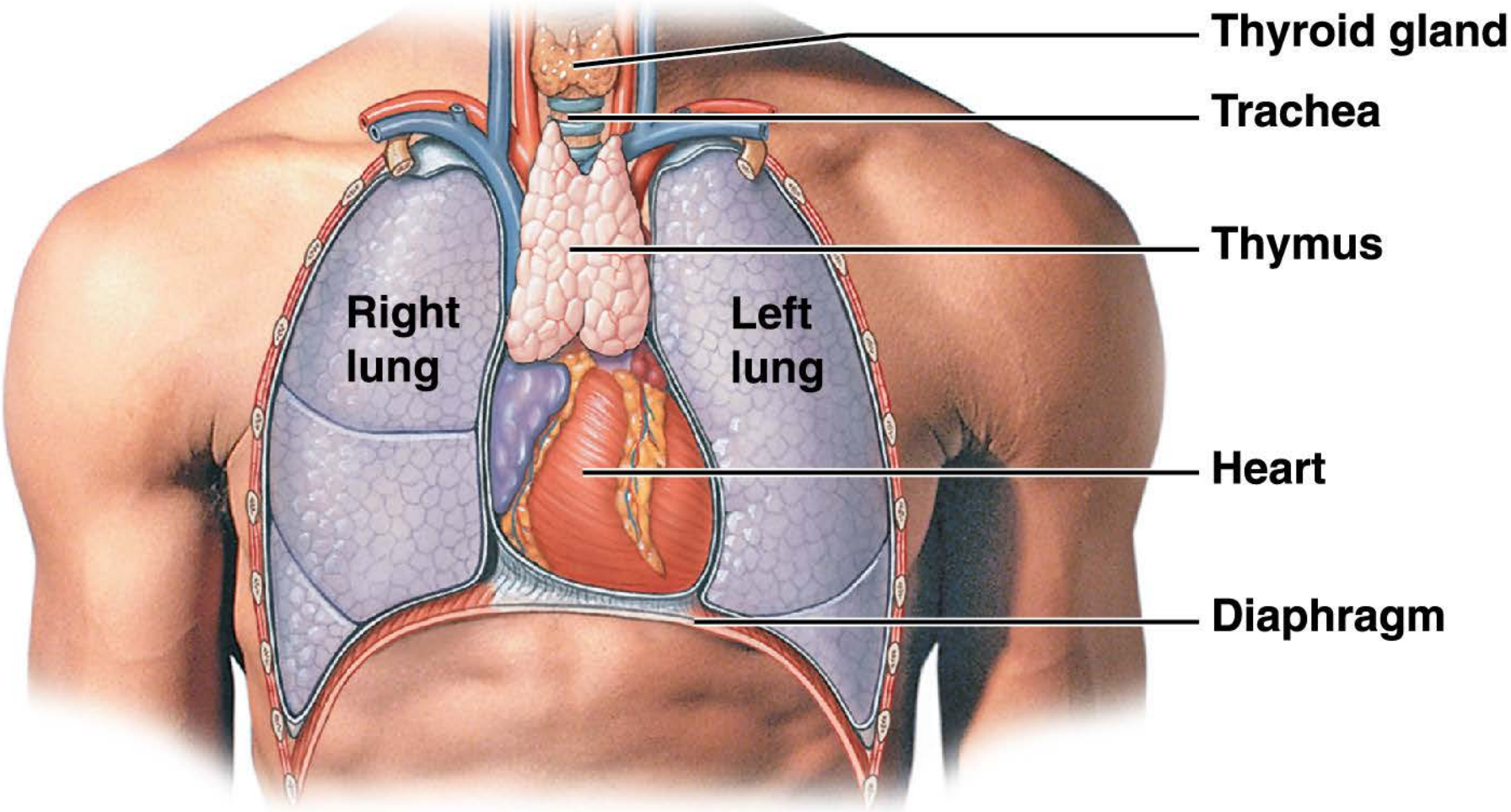
Thymus



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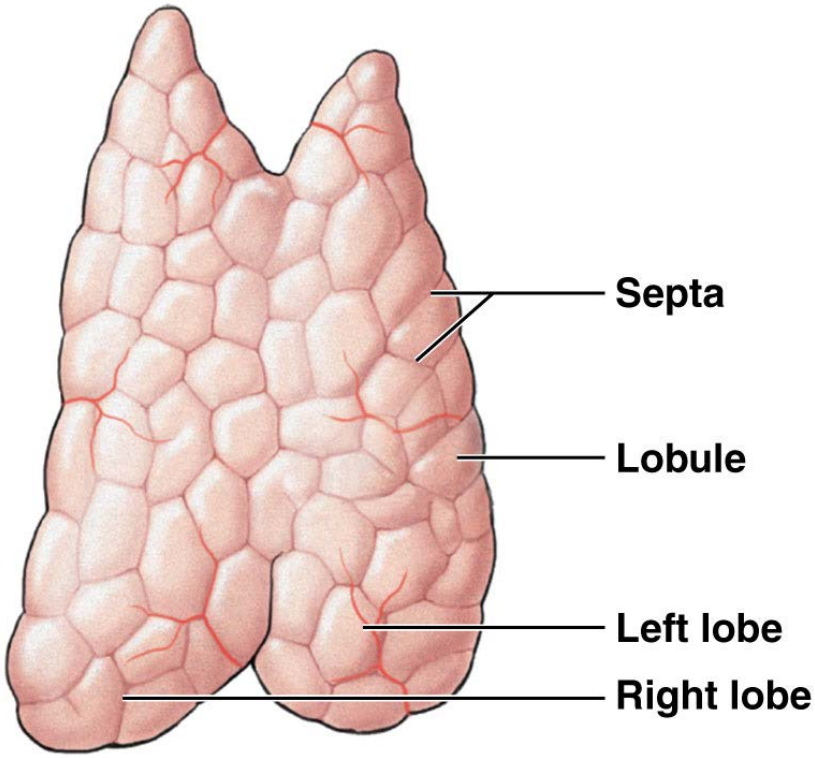
Module 20.6: The thymus

Thymus description

- Located in the mediastinum
  - Posterior to the sternum
- Covered in a capsule that divides it into left and right **lobes**
  - Fibrous partitions (**septa**) divide the lobes into **lobules**
    - Each lobule is about 2 mm in diameter



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Module 20.6: The thymus

Thymus histology

Each lobule consists of:

- Dark outer **cortex**
  - Contains dividing lymphocytes arranged in clusters surrounded by **epithelial reticular cells** (**ERCs**)
    - Regulate T cell development and function
  - Blood vessels in the cortex are also surrounded by epithelial cells
    - Maintain the **blood thymus barrier**
- Lighter central **medulla**

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Module 20.6: The thymus

Thymus histology (continued)

- Developing T cells leave the cortex after about 3 weeks and enter the **medulla**
  - No blood thymus barrier in medulla
    - Developing T cells may enter medullary blood vessel
    - May also enter a lymphatic vessel and leave the thymus through an efferent lymphatic
  - Thymic epithelial cells form **thymic corpuscles**
    - Distinctively shaped clusters of cells in concentric layers

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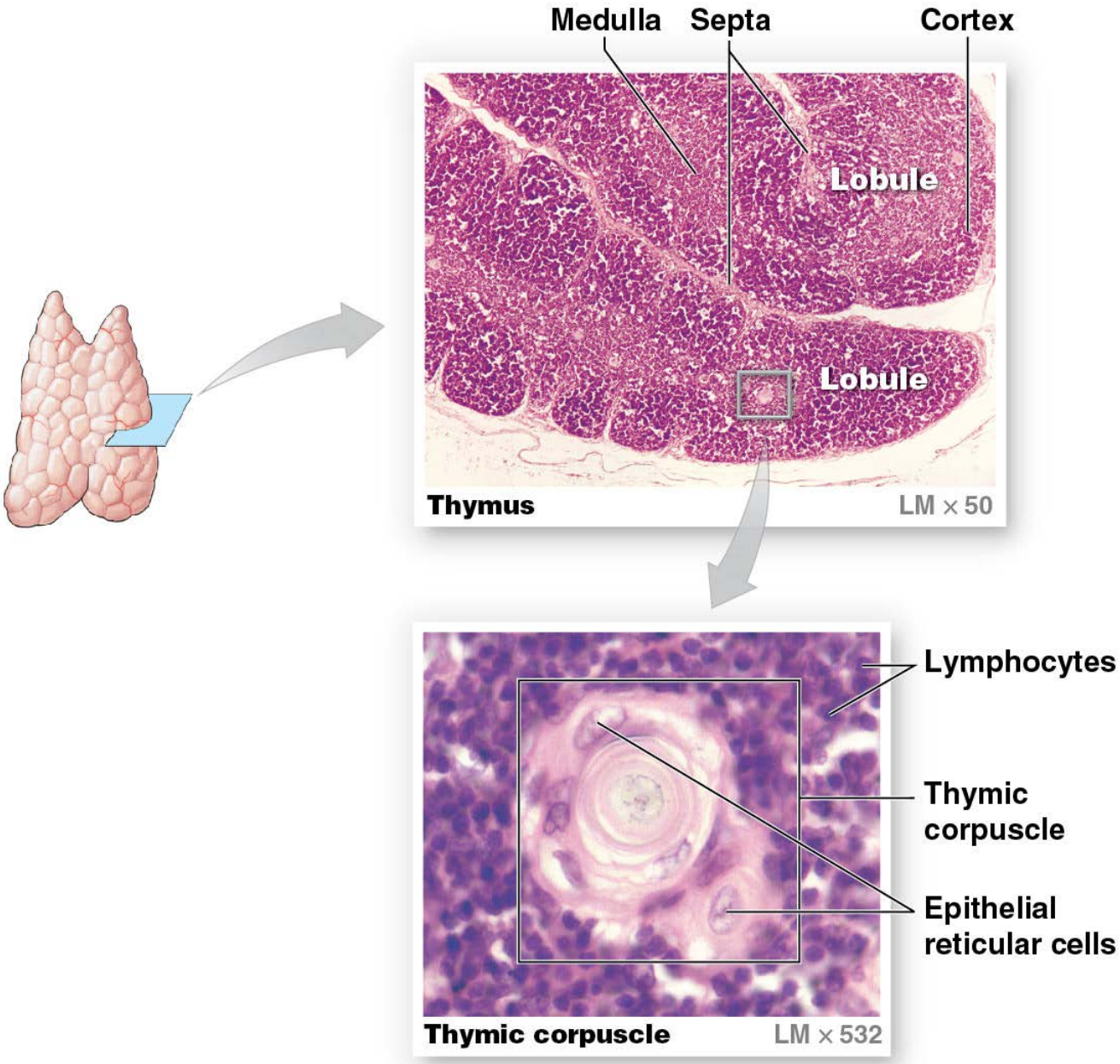
Thymus Histology



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Module 20.6: The thymus

Myasthenia gravis

- Autoimmune disease associated with enlarged, hyperactive thymus
- Characterized by skeletal muscle weakness
- Acetylcholine (ACh) receptors at neuromuscular junction are destroyed, altered, or blocked by self antibodies

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Module 20.6: Review

A. Where is the thymus located?
B. Describe the gross anatomy of the thymus.
C. Which cells maintain the blood thymus barrier?

Learning Outcome: Describe the structure and function of the thymus.

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Module 20.7: The spleen, the largest lymphoid organ, responds to antigens in the bloodstream

Spleen

- Contains the largest mass of lymphoid tissue in the body
- Performs same function for blood that lymph nodes do for lymph (filter)
  1. Removes abnormal red blood cells and other blood components by phagocytosis
  2. Stores iron recycled from red blood cells
  3. Initiates immune response by B cells and T cells in response to antigens in circulating blood

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Module 20.7: The spleen

Gross anatomy of the spleen

- Lies along the curving lateral border of the stomach on the left side
  - Attached to lateral border of the stomach by the **gastrosplenic ligament** (broad band of mesentery)
- **Diaphragmatic surface**
  - Smooth and convex
  - Conforms to the shape of the diaphragm and the body wall

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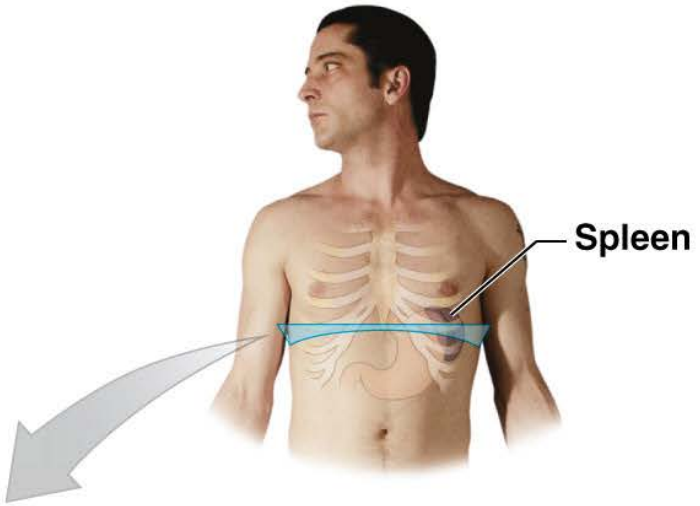
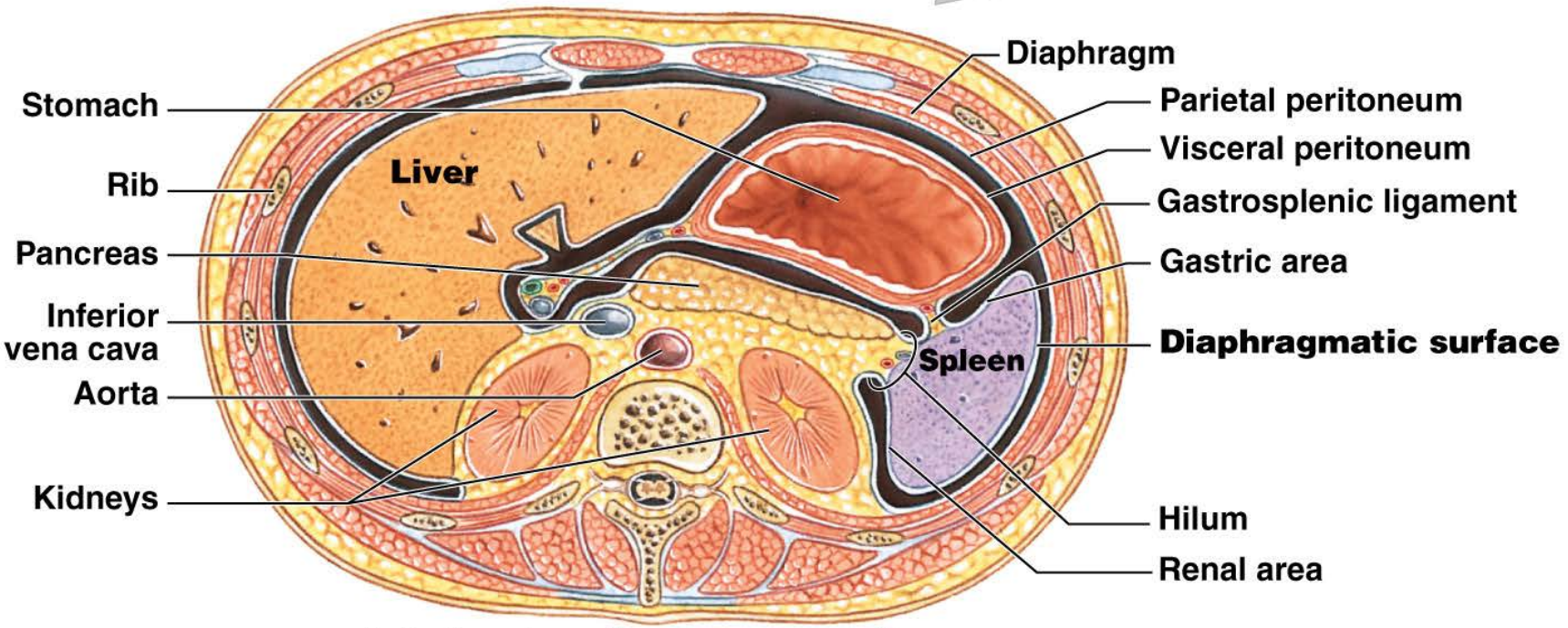
The Spleen





Inferior view, transverse section

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Module 20.7: The spleen

Gross anatomy of the spleen (continued)

- About 12 cm (5 in.) long and weighs ~160 g (5.6 oz.)
- Deep red when dissected
  - Due to large amounts of blood it contains
- Soft texture
  - Shape molded by structures around it
  - **Visceral** (medial) **surface** has two indentations
    - **Gastric area** (near stomach)
    - **Renal area** (near kidney)
- **Hilum** (indentation where blood and lymphatic vessels communicate)

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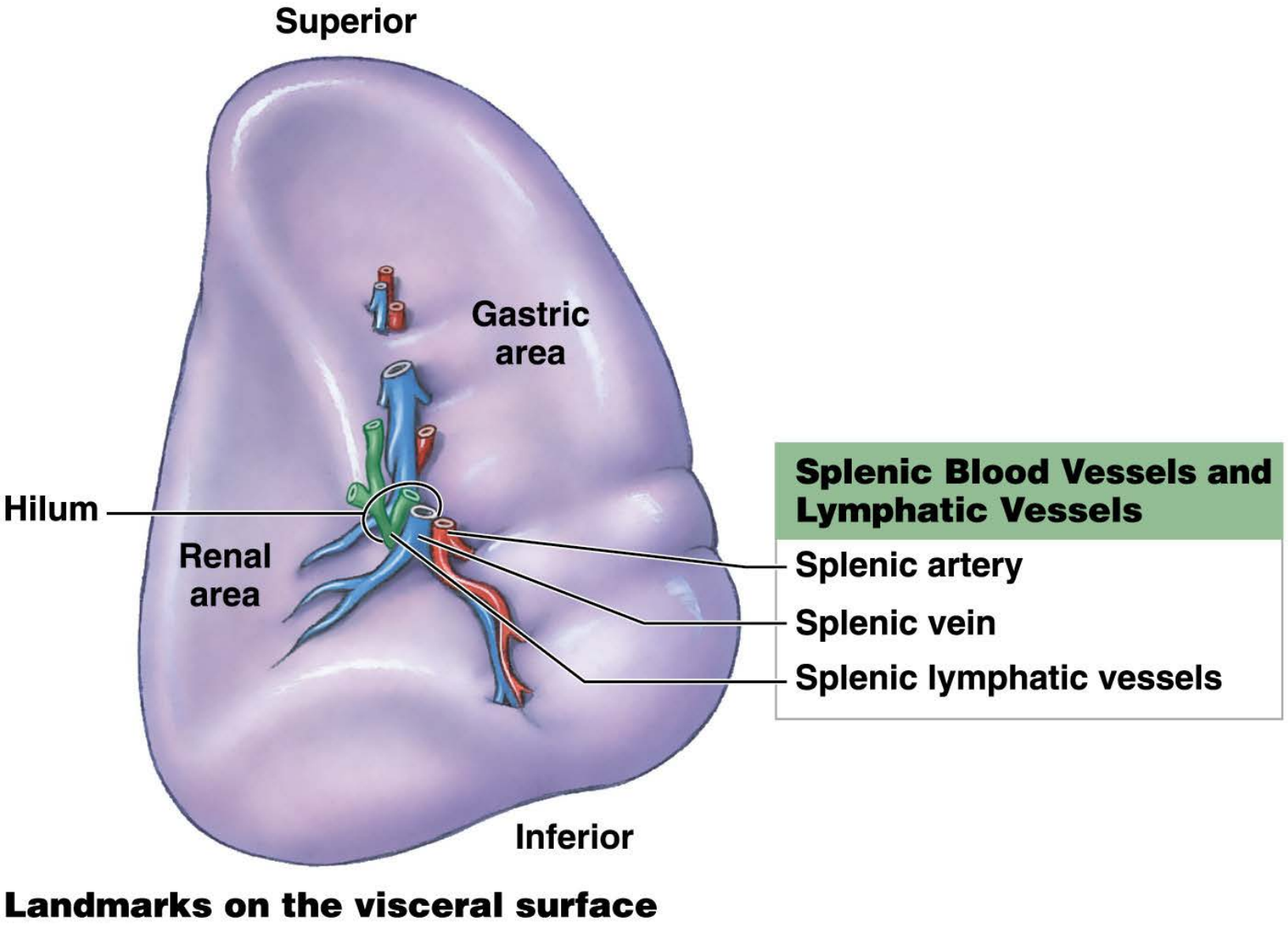
Spleen anatomy



Landmarks on the visceral surface

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Module 20.7: The spleen

Internal anatomy

- Outer capsule of collagen and elastic fibers
  - Fairly easily ruptured by impact
  - Spleen tissue too fragile to repair surgically
  - Damage can necessitate removal (**splenectomy**)
- **Trabeculae**
  - Fibrous partitions that radiate outward from the hilum toward the capsule
  - Allow room for blood vessels

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Module 20.7: The spleen

Internal anatomy (continued)

- **Pulp**
  - Cellular components within the capsule
  - Allow identification and removal of microorganisms and damaged or infected cells in bloodstream
  - **Red pulp**
    - Contains large quantities of RBCs
    - Also contains macrophages
  - **White pulp**
    - Resembles lymphoid nodules with lymphocytes

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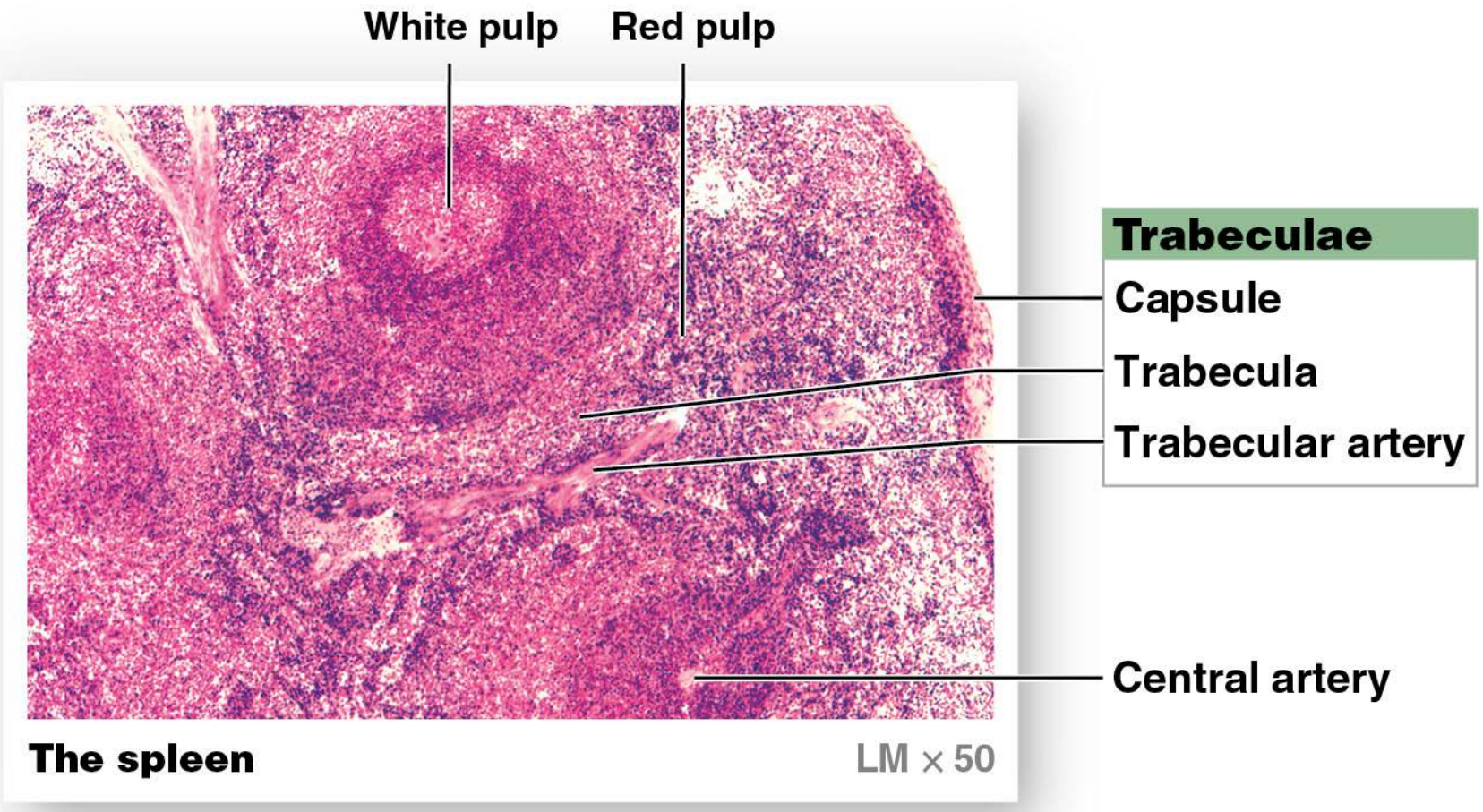
Internal anatomy of the spleen



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Blood flow through the spleen

Path of Blood Flow through the Spleen

The **trabecular arteries** are branches of the splenic artery. Their finer branches, called **central arteries**, are surrounded by areas of white pulp.	Capillaries discharge the blood into the reticular tissue of the red pulp, which contains free and fixed macrophages.	Blood flows into sinusoids (see Module 19.3), whose walls contain fixed macrophages.	Blood collects into small veins that in turn merge to form **trabecular veins** that unite at the hilum.

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Module 20.7: The spleen

A ruptured spleen is a medical emergency

- Spleen tears easily and is difficult to repair surgically
- **Splenectomy**—removal of spleen
- Without a spleen, person has increased risk for bacterial infection

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Module 20.7: Review

A. What are the functions of the spleen?
B. Describe red pulp and white pulp found in the spleen.
C. Beginning at the trabecular arteries, trace the path of blood through the spleen.

Learning Outcome: Describe the structure and function of the spleen, and trace blood flow through it.

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Section 2: Innate immunity

Learning Outcomes

20.8 Give an overview of the components of innate (nonspecific) immunity.

20.9 Explain how physical barriers play a role in innate immunity.

20.10 Explain the role phagocytes play in innate immunity.

20.11 Describe immune surveillance, and explain the role of NK cells.

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Section 2: Innate immunity

Learning Outcomes (continued)

20.12 Describe the types of interferons, and explain the pathways of complement activation.

20.13 Explain the significance of inflammation and fever as innate defense mechanisms.

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Module 20.8: Innate immunity is nonspecific and is not stimulated by specific antigens

Immunity

- The ability to fight infection, illness, and disease
- Two complementary mechanisms work independently and together as the **immune response**
  1. **Innate** (**nonspecific**) **immunity**
     - Does not distinguish one type of threat from another
     - Response is the same regardless of type of invading agent
     - Present at birth (innate)
     - Provides **nonspecific resistance**
     - Prevents the approach, denies the entry, limits the spread of microbes or other environmental hazards

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Module 20.8: Innate immunity

Immunity (continued)

- Two mechanisms of immunity (continued)
  1. **Innate** (**nonspecific**) **immunity** (continued)
     - **Physical barriers**—skin and mucous membranes
     - **Phagocytes**—cells that engulf pathogens and cell debris
     - **Immune surveillance**—destruction of abnormal cells by natural killer (NK) cells
     - **Interferons**—chemicals against viral infections
     - **Complement**—circulating proteins that assist antibodies
     - **Inflammation**—localized tissue-level response to limit spread of infection
     - **Fever**—elevation of body temperature

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Module 20.8: Innate immunity

Immunity (continued)

- Two mechanisms of immunity (continued)
  2. **Adaptive** (**specific**) **immunity**
     - Utilizes **adaptive defenses**
     - Protects against particular threats
     - Depends on the activities of specific lymphocytes
     - Produces state of protection known as **specific resistance**

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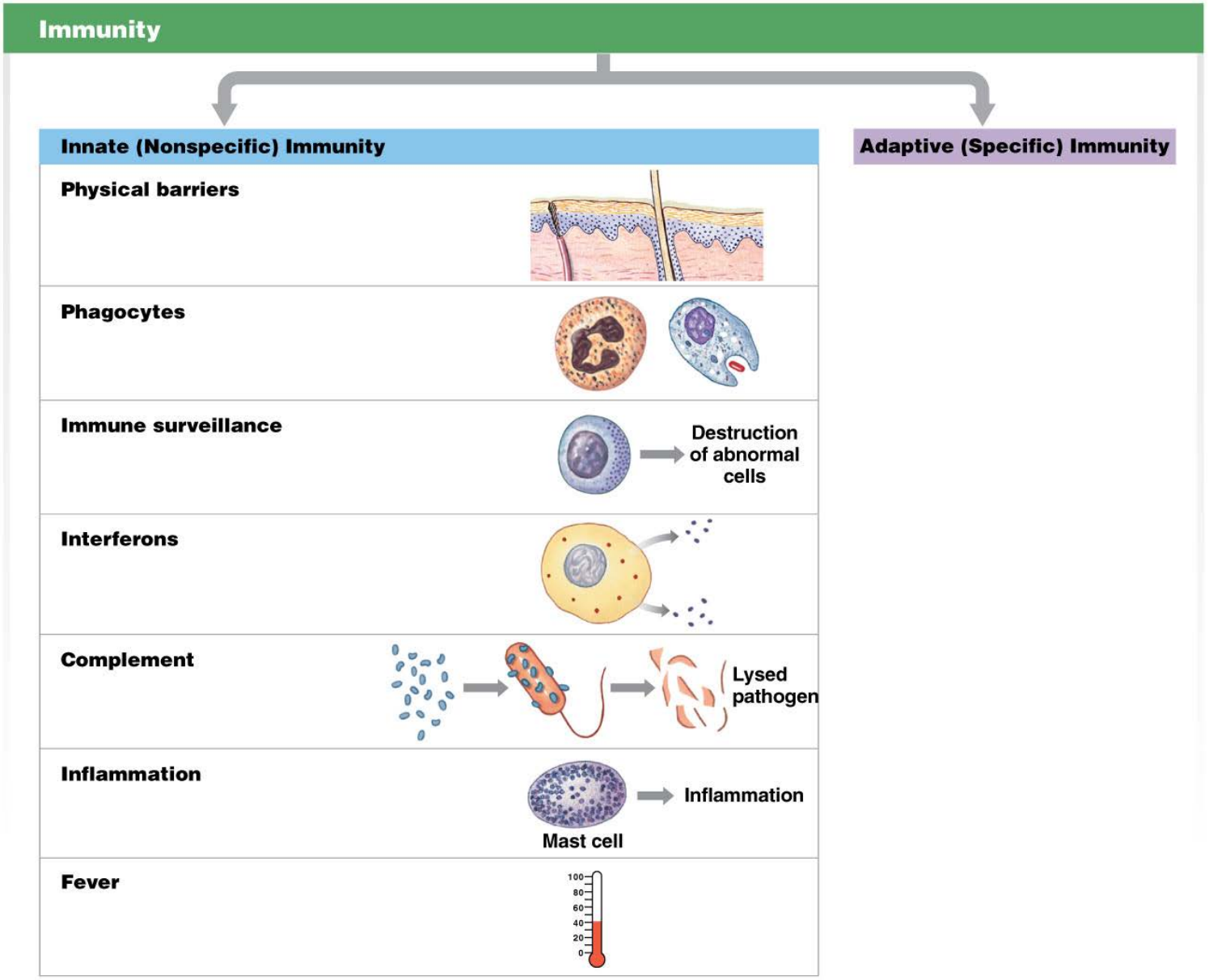
Immunity



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Module 20.8: Review

A. Distinguish between innate immunity and adaptive immunity.
B. How does innate immunity protect us from disease?
C. A child falls off her bike and skins her knee. Which form of immunity will be activated immediately?

Learning Outcome: Give an overview of the components of innate (nonspecific) immunity.

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Module 20.9: Physical barriers prevent pathogens and toxins from entering body tissues

Physical barriers

- Integumentary system
  - Secretions
    - From sebaceous and sweat glands wash away microorganisms and chemical agents
    - May also contain bactericidal chemicals, destructive enzymes (lysozymes), and antibodies

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Module 20.9: Physical barriers

Physical barriers (continued)

- Integumentary system (continued)
  - Hair
    - Provides protection from physical abrasion
    - Prevents hazardous materials or insects from contacting skin
  - Stratified squamous epithelium
    - Multiple layers of epithelial cells with keratin that are connected with desmosomes

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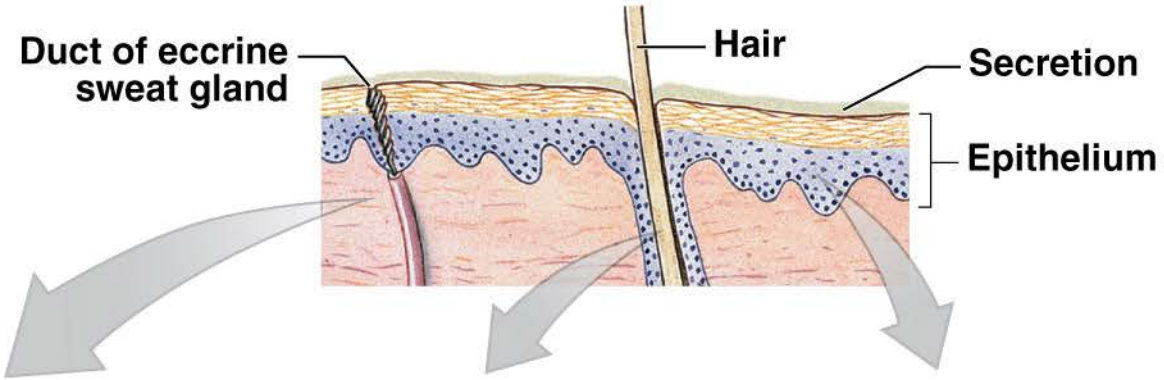
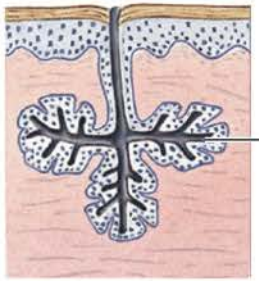
Integumentary system and innate immunity

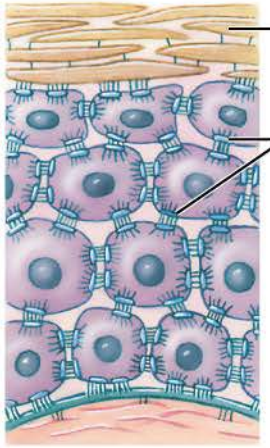


Secretions



Hair

Stratified squamous epithelium



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Module 20.9: Physical barriers

Physical barriers (continued)

- Other epithelial linings
  - Found along digestive, respiratory, urinary, and reproductive tracts
  - Cells provide physical barrier
  - Secretions (mucus, enzymes, stomach acid) often ensnare, destroy, or wash away pathogenic material
  - MALT provides nonspecific defense

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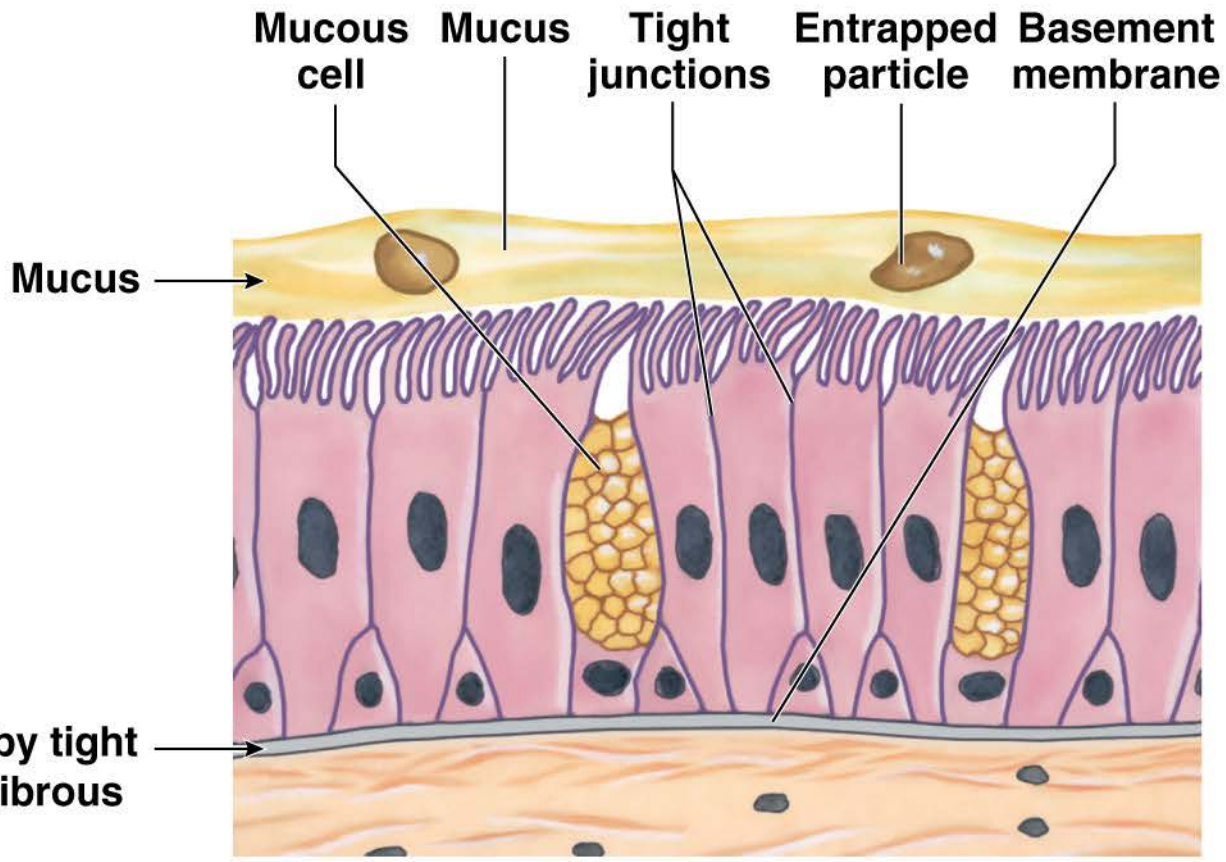
Mucous membranes



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Module 20.9: Review

A. How does the integumentary system protect the body?

Learning Outcome: Explain how physical barriers play a role in innate immunity.

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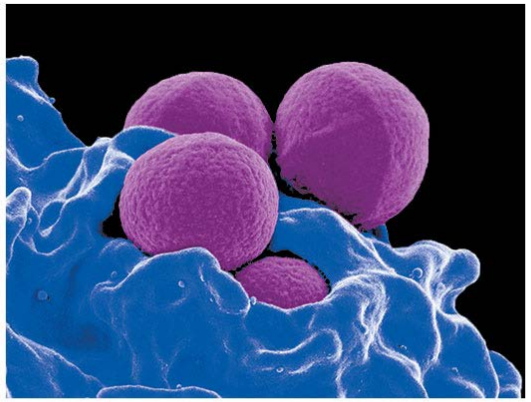
Module 20.10: Phagocytes respond to pathogen invasion

Phagocytes



Phagocyte engulfing bacteria SEM × 2900

- Engulf and destroy foreign substance, pathogens, and cellular debris
- "First line of cellular defense" against pathogenic invasion
  - Can attack and remove microorganisms even before lymphocytes detect their presence
- Different types target different threats
  - All function in the same basic way

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Module 20.10: Phagocytes

Phagocytes (continued)

- **Neutrophils** (in bloodstream and tissues)
  - Abundant, mobile, fast-acting
  - Phagocytize cellular debris or bacteria
- **Eosinophils** (less abundant than neutrophils)
  - Phagocytize foreign compounds and antibody-coated pathogens

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Module 20.10: Phagocytes

Phagocytes (continued)

- **Monocyte–macrophage** system (reticuloendothelial system)
  - **Macrophages** (derived from monocytes)
    - **Fixed macrophages** (scattered among connective tissues; immobile within those tissues)
    - **Free macrophages** (travel throughout body)

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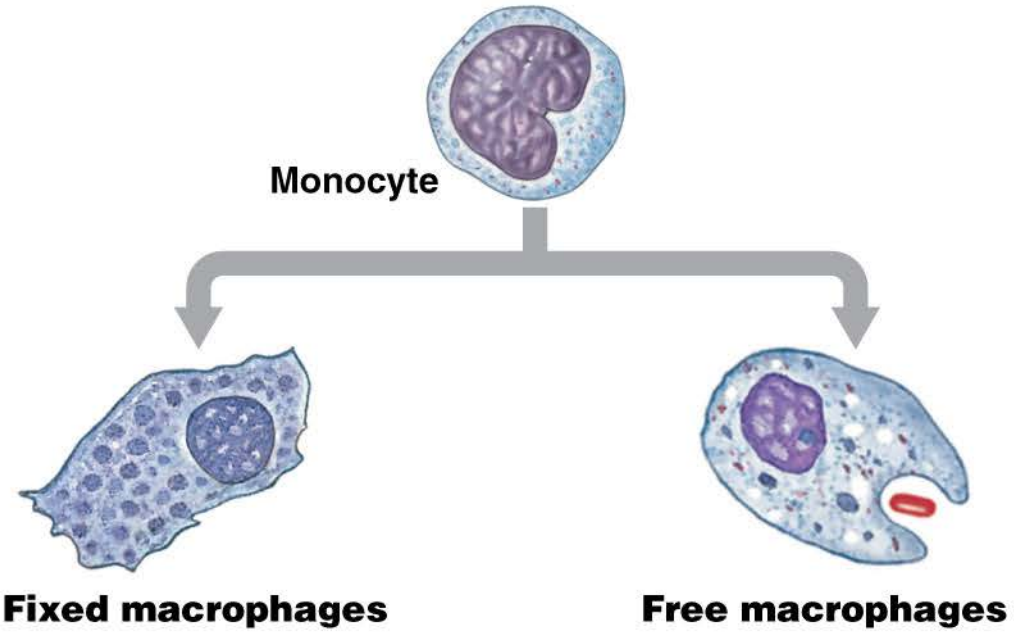
Types of phagocytes

Types of Phagocytes

Neutrophils	Eosinophils	Macrophages
12 µm	8–10 µm	 Monocyte; Fixed macrophages; Free macrophages

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Functional Characteristics of Phagocytes

- Phagocytes can leave capillaries by squeezing between adjacent endothelial cells, a process known as **emigration**.
- Phagocytes may be attracted to or repelled by chemicals in the surrounding fluids, a phenomenon called **chemotaxis**. They are particularly sensitive to chemicals released by body cells or pathogens.
- Phagocytosis always begins with **adhesion**, the attachment of the phagocyte to its target. In this process, receptors on the plasma membrane of the phagocyte bind to the surface of the target.
- After adhesion, the phagocyte may either destroy the target itself or promote its destruction by activating specific defenses.

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Module 20.10: Review

A. Identify the types of phagocytes in the body, and differentiate between fixed macrophages and free macrophages.
B. Define *chemotaxis*.

Learning Outcome: Explain the role phagocytes play in innate immunity.

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Module 20.11: NK cells perform immune surveillance, detecting and destroying abnormal cells

Immune surveillance

- Constant monitoring of normal tissues (**immune surveillance**) by **natural killer** (**NK**) cells
  - Normal cells are generally ignored by immune system
  - Cancer cells often contain **tumor-specific antigens**
    - NK cells recognize as abnormal and destroy
  - NK cells recognize bacteria, foreign cells, virus-infected cells, and cancer cells

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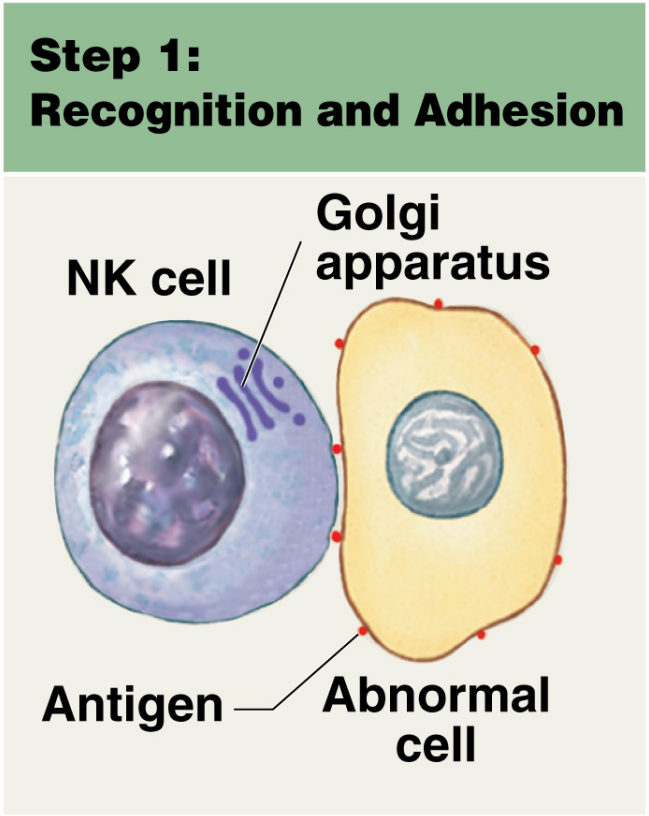
Module 20.11: Immune surveillance

Steps of NK recognition and destruction

1. Presence of unusual plasma membrane activates NK cell
   - NK cell adheres to target cell



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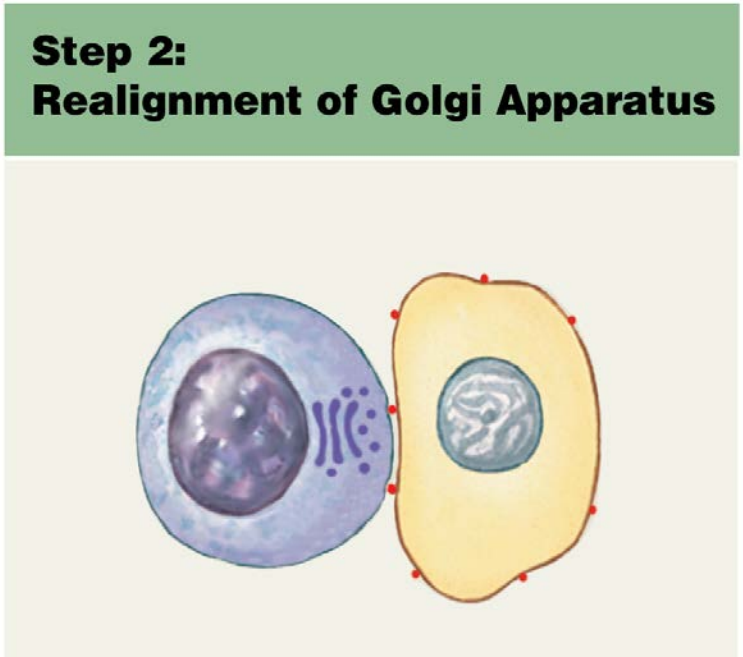
Module 20.11: Immune surveillance

Steps of NK recognition and destruction (continued)

2. Golgi apparatus moves within NK cell near target cell
   - Produces many secretory vesicles containing **perforins**



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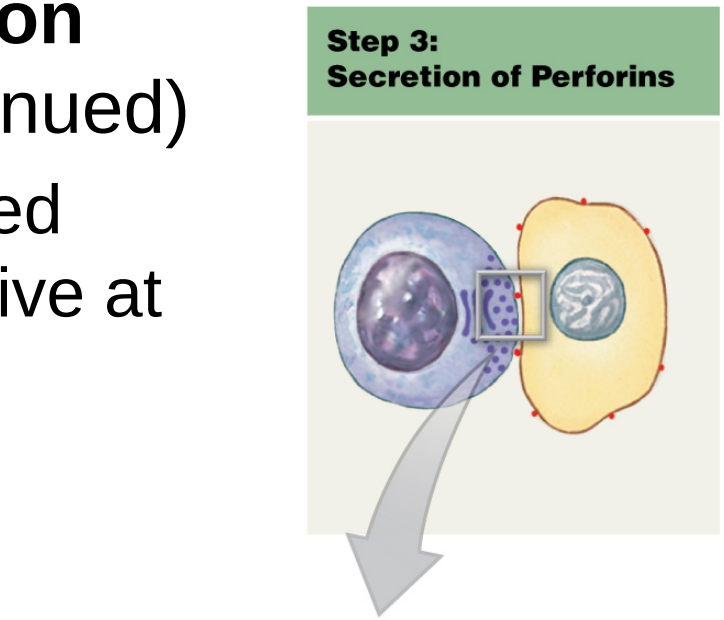
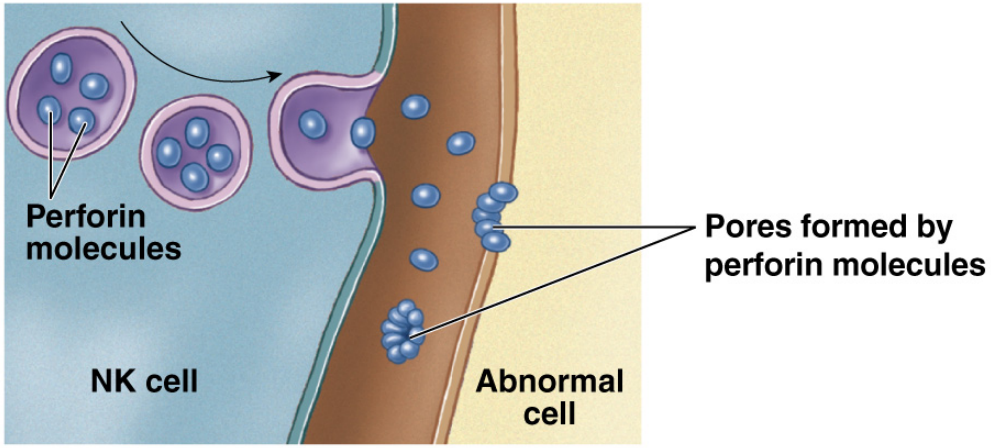
Module 20.11: Immune surveillance

Steps of NK recognition and destruction (continued)

3. Perforins are released from NK cell and arrive at target cell





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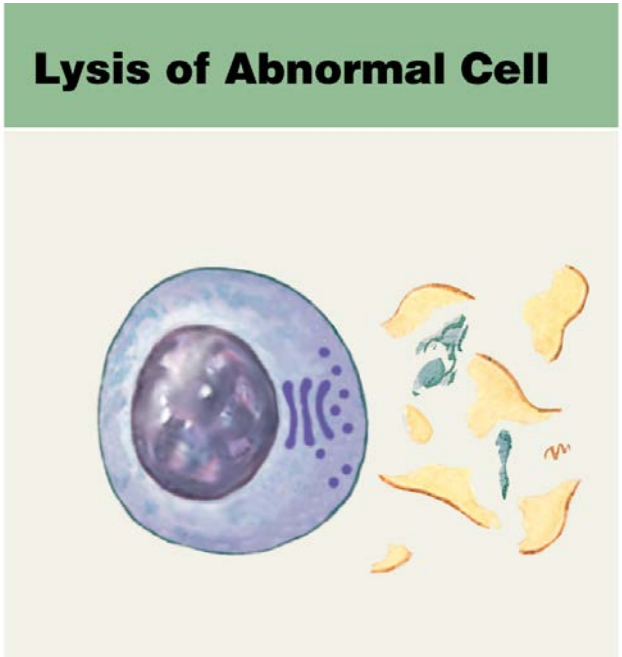
Module 20.11: Immune surveillance

Steps of NK recognition and destruction (continued)

4. Perforins create pores in target cell membrane
   - Target cell can no longer maintain its internal environment and disintegrates



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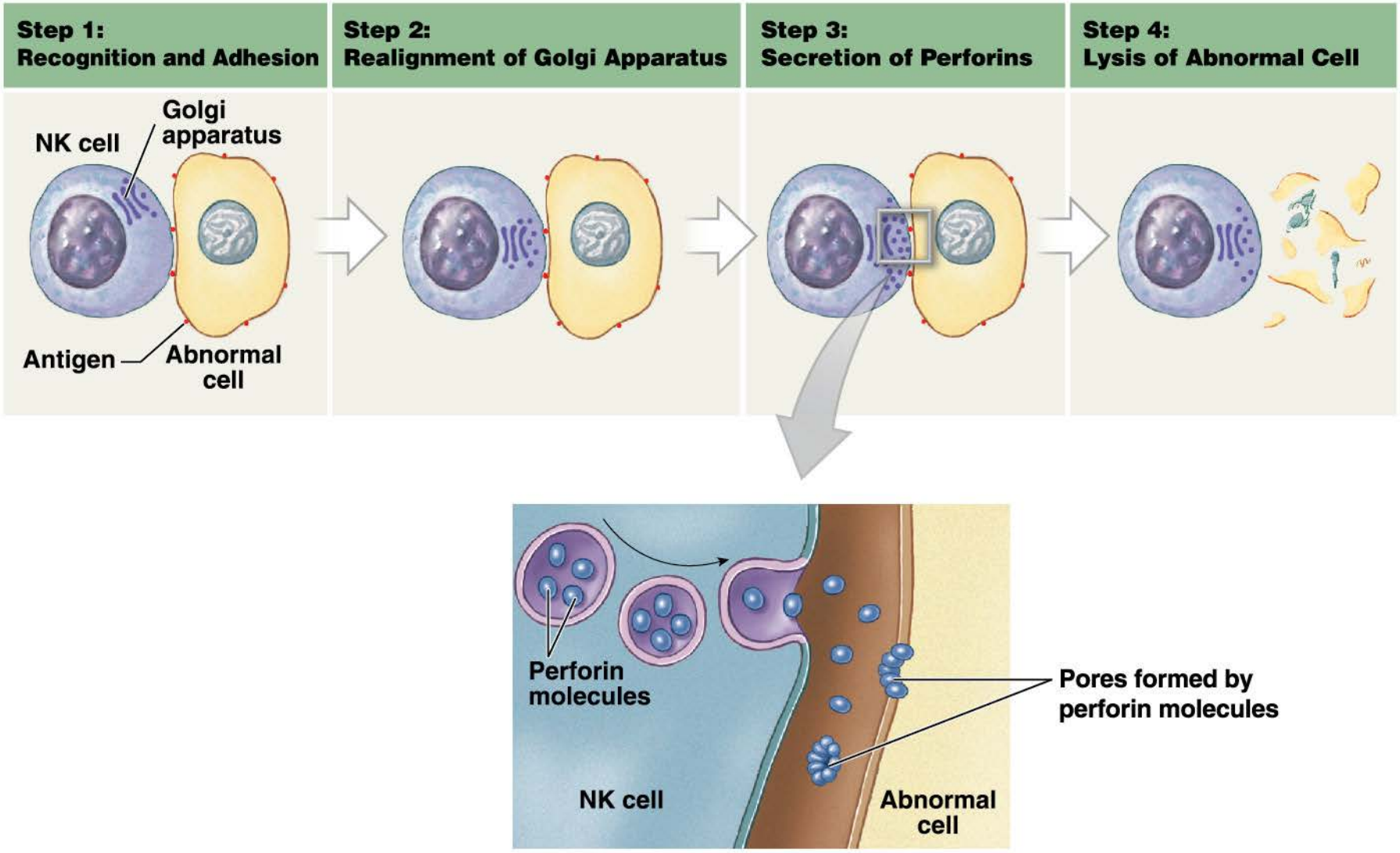
NK Cells



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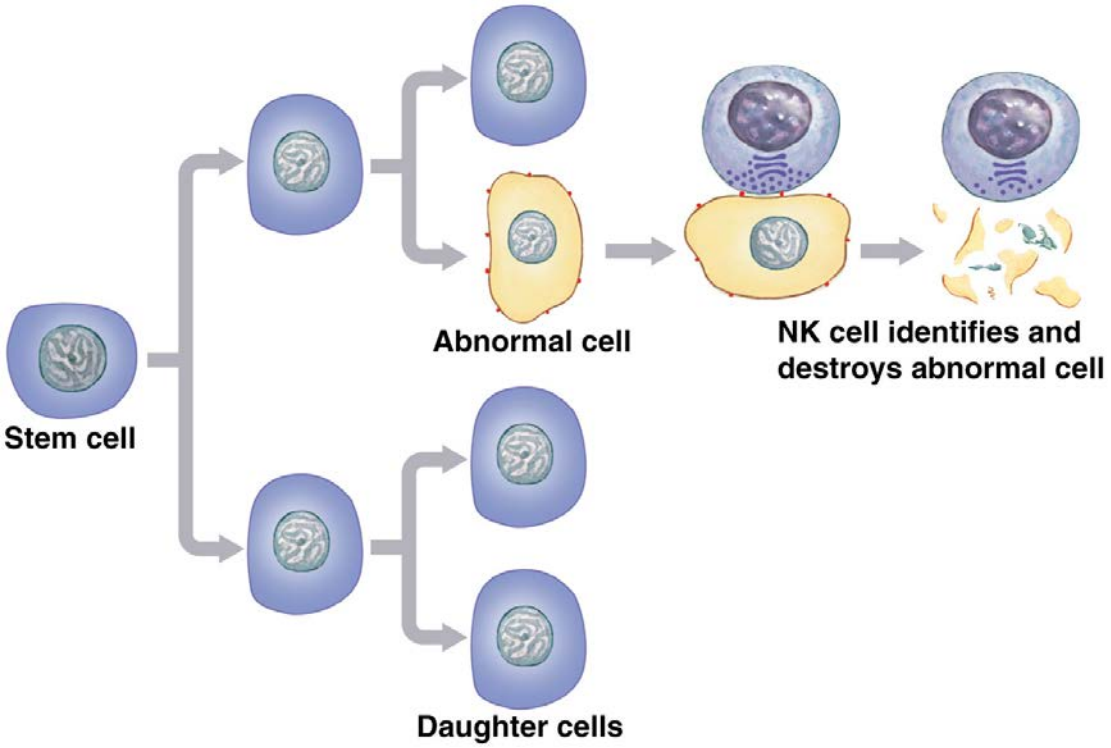
Module 20.11: Immune surveillance

Mistakes in cell division

- NK cells also destroy abnormal cells
  - Abnormal daughter cells occur during cell division
  - Some abnormal cells become cancer cells



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Module 20.11: Immune surveillance

Immunological escape

- Immune surveillance by NK cells is not perfect
  - Primary tumors may be surrounded by a capsule and escape detection
    - Released malignant cells may be detected and destroyed
  - Daughter tumor cells sometimes do not display tumor-specific antigens or secrete chemicals that kill NK cells
    - Cancer cells can spread and create secondary tumors

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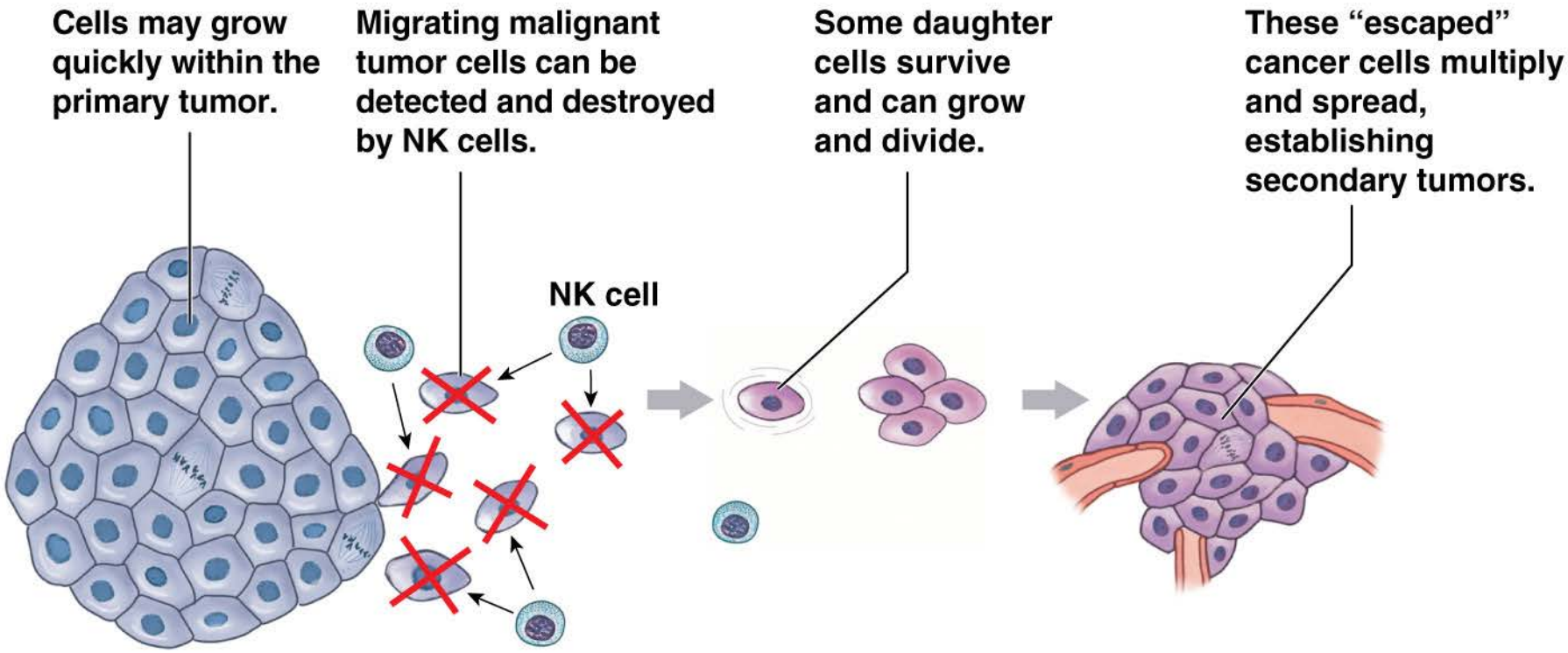
Immunological escape



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Module 20.11: Review

A. Define *immune surveillance*.
B. How do NK cells detect cancer cells?
C. If NK cells are engaged in immune surveillance, how do cancer cells spread?

Learning Outcome: Describe immune surveillance, and explain the role of NK cells.

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Module 20.12: Interferons and the complement system are distributed widely in body fluids

Interferons (**IFNs**)

- Small proteins released by activated lymphocytes, macrophages, and virus-infected tissues
- Trigger production of **antiviral proteins** in cytoplasm of nearby cells
  - Do not prevent entry of viruses but interfere with viral replication
- Also stimulate activities of macrophages and NK cells
- *Examples* of **cytokines**
  - Chemicals released by cells to coordinate local activities

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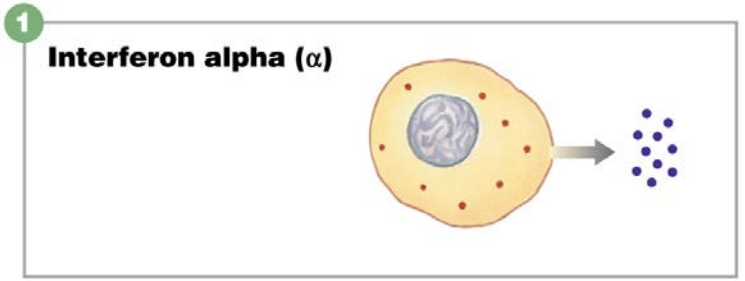
Module 20.12: Interferons and the complement system

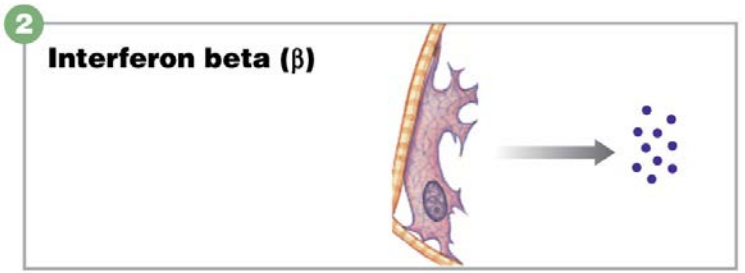
Interferons (continued)

- **Three types**

1. **Interferon alpha (α)**
   - Produced by virus-infected cells
   - Attract and stimulate NK cells and enhance resistance to viral infection



2. **Interferon beta (β)**
   - Secreted by fibroblasts
   - Slow inflammation in damaged area



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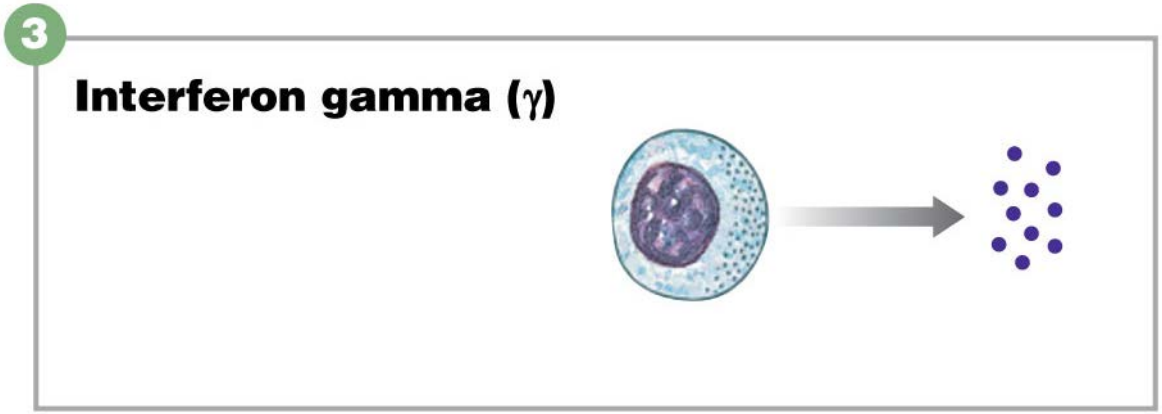
Module 20.12: Interferons and the complement system

Interferons (continued)

- **Three types** (continued)
  3. **Interferon gamma** (γ)
     - Secreted by T cells and NK cells
     - Stimulate macrophage activity



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Module 20.12: Interferons and the complement system

Complement system

- Name refers to the fact that the system *complements* the action of antibodies
- Over 30 special proteins form this system
  - Proteins interact with one another in chain reactions or cascades (similar to blood clotting system)
- Three possible pathways
  1. **Classical pathway**
  2. **Lectin pathway**
  3. **Alternative pathway**

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Module 20.12: Interferons and the complement system

Complement system (continued)

1. The classical pathway
   - Most rapid and effective complement activation method
   - Complement proteins attach to antibody molecules already bound to a pathogen
   - Attached protein activates and initiates cascade to activate and attach other complement proteins
   - **Membrane attack complex** (**MAC**)—destroys integrity of target cell

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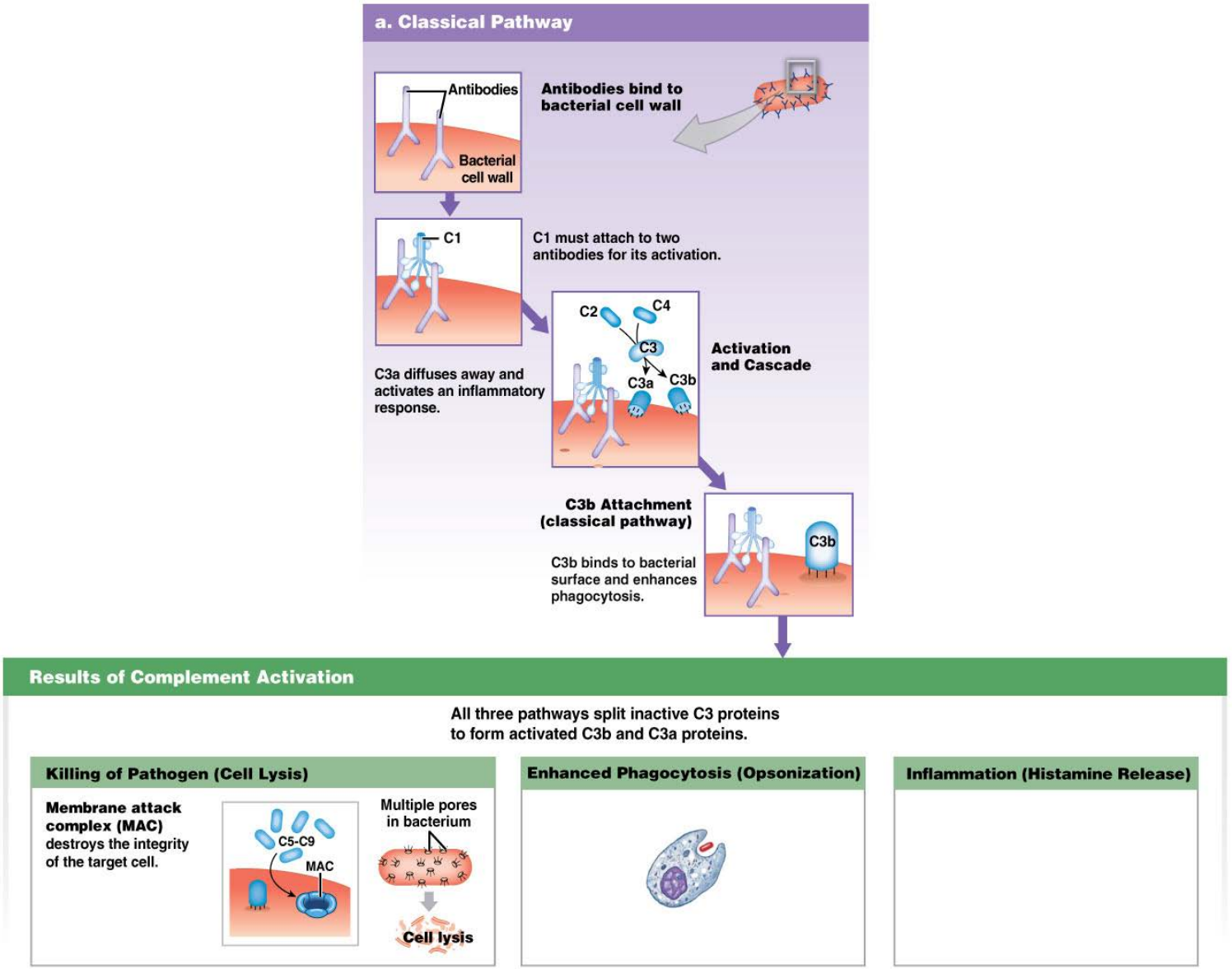
Classical pathway



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Module 20.12: Interferons and the complement system

Complement system (continued)

2. The lectin pathway
   - Activated by mannose-binding lectin (MBL) protein
     - Binds to carbohydrates on bacterial surfaces
   - Activates an inflammatory response
   - Also enhances phagocytosis (**opsonization**)

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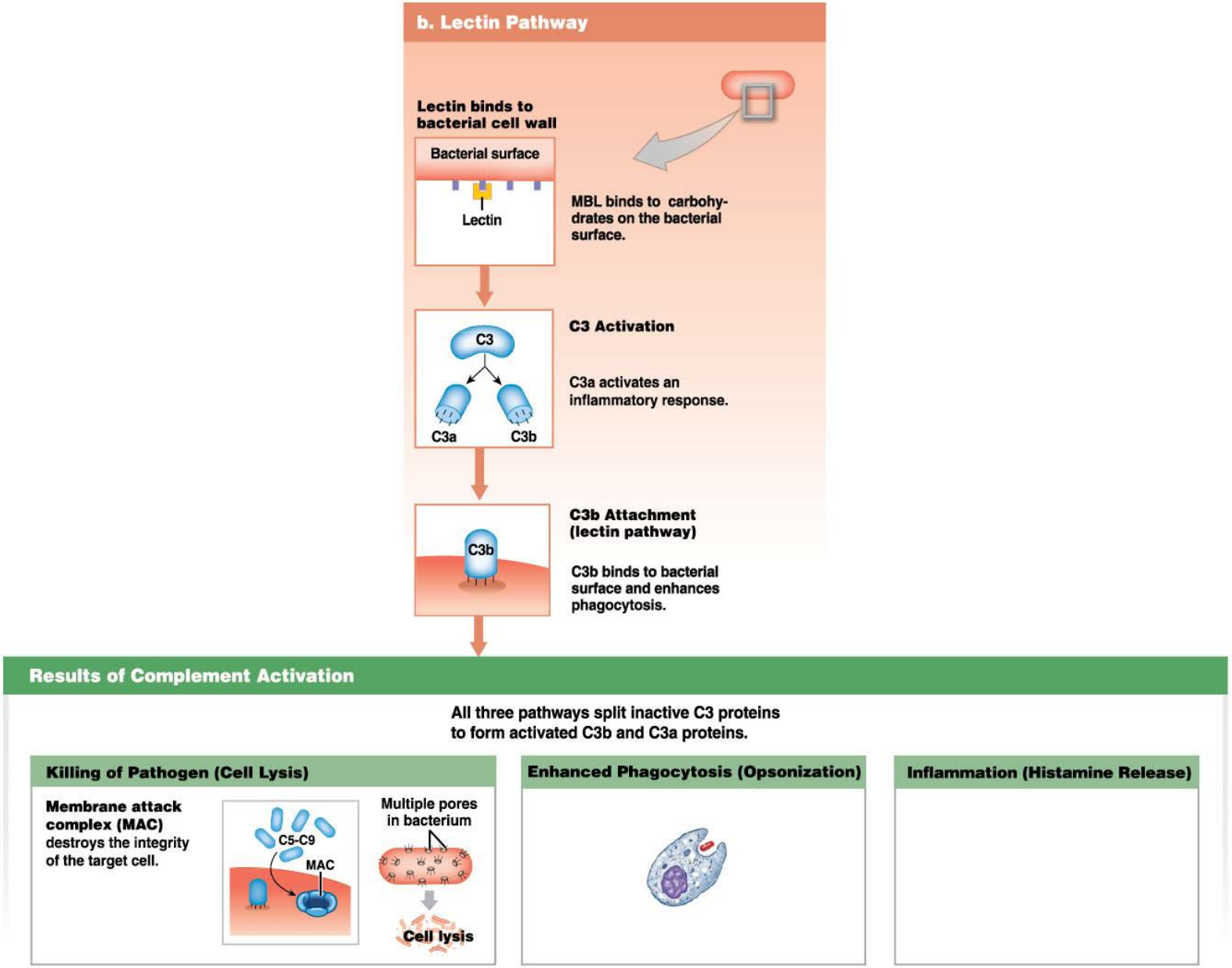
Lectin pathway



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Module 20.12: Interferons and the complement system

Complement system (continued)

3. The alternative pathway
   - Important defense against bacteria, some parasites, and virus-infected cells
   - Several complement proteins (notably properdin) interact in the plasma
     - Interaction triggered by exposure to foreign substances
   - End result is attachment of activated complement protein

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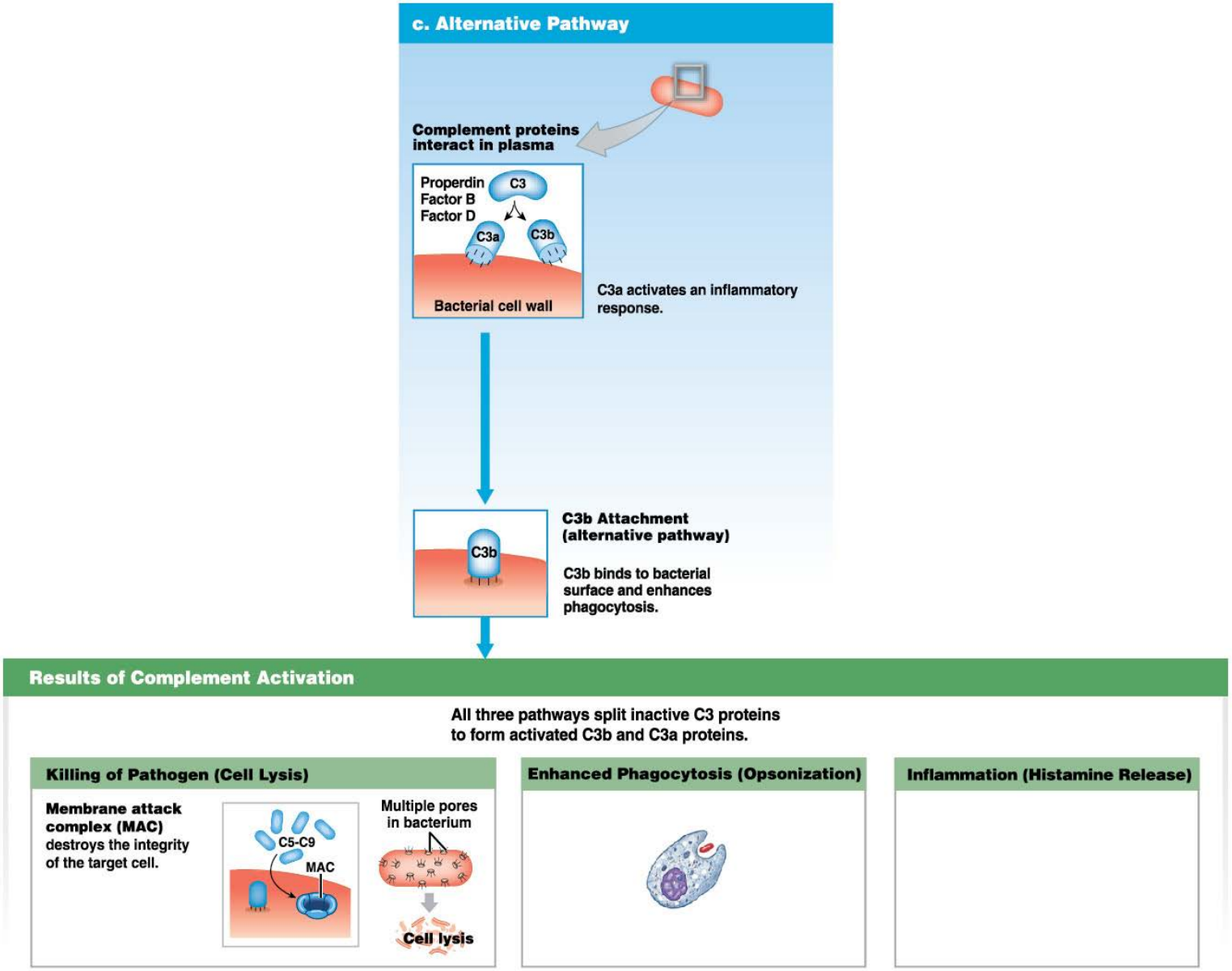
Alternative pathway



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Module 20.12: Interferons and the complement system

Complement system (continued)

- Regardless of the pathway, the effects are the same
- **Pore formation and cell lysis**
  - Pore formed in cell membrane by many complement proteins
  - Destroys integrity of target cell

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Module 20.12: Interferons and the complement system

Complement system (continued)

- **Enhanced phagocytosis**
  - Attracts phagocytes and makes target cells easier to engulf
  - Process called **opsonization**
- **Histamine release**
  - By mast cells and basophils
  - Increases inflammation and blood flow to region

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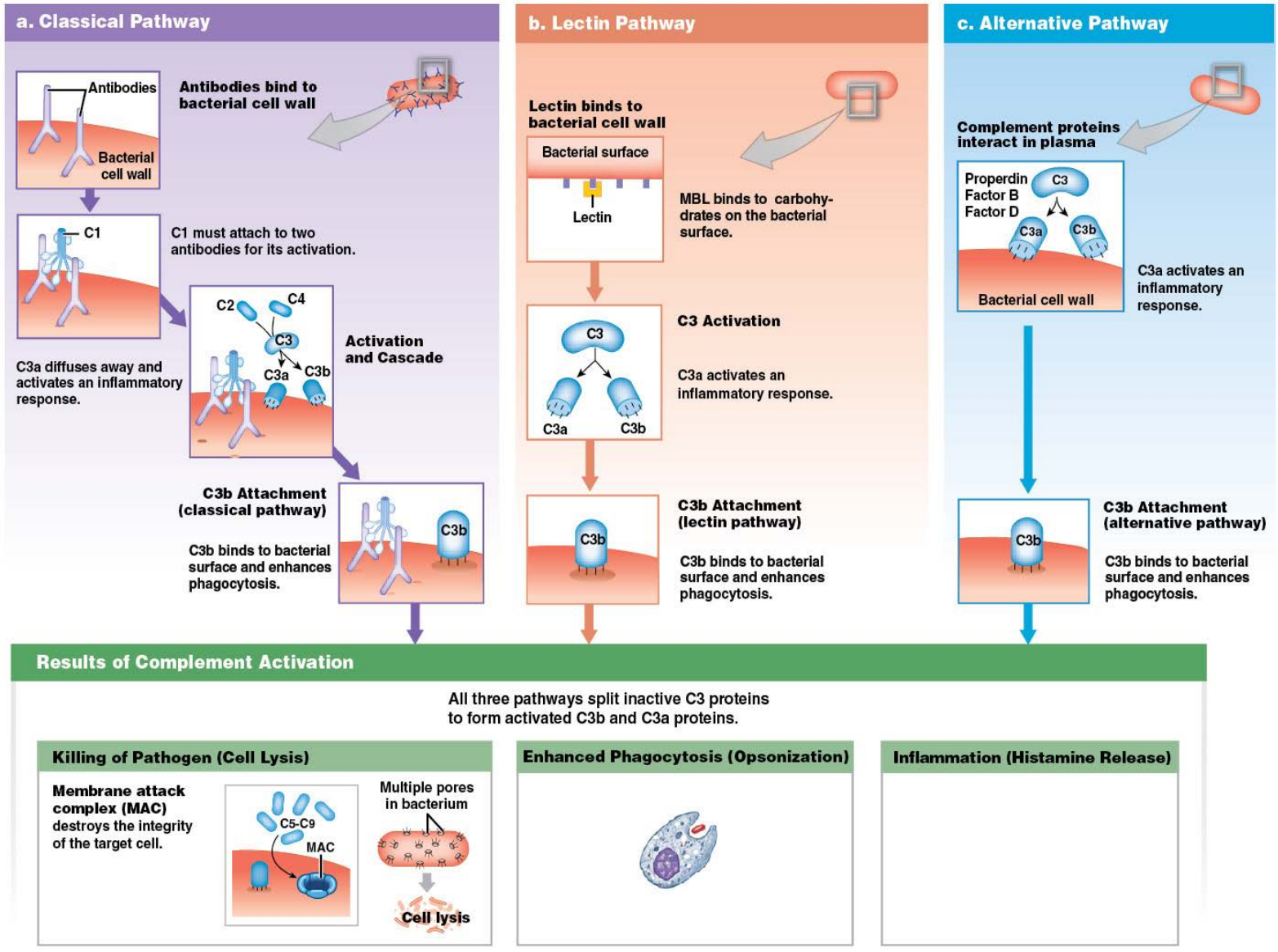
Complement system



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Module 20.12: Review

A. Define *interferons*.
B. Briefly explain the role of complement proteins.
C. What is the effect of histamine release?

Learning Outcome: Describe the types of interferons, and explain the pathways of complement activation.

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Module 20.13: Inflammation is a localized tissue response to injury; fever is a generalized response to tissue damage and infection

Inflammation, or inflammatory response

- Localized tissue response to injury, producing the cardinal signs and symptoms of inflammation
  - Local redness
  - Swelling
  - Heat
  - Pain
  - Sometimes lost function

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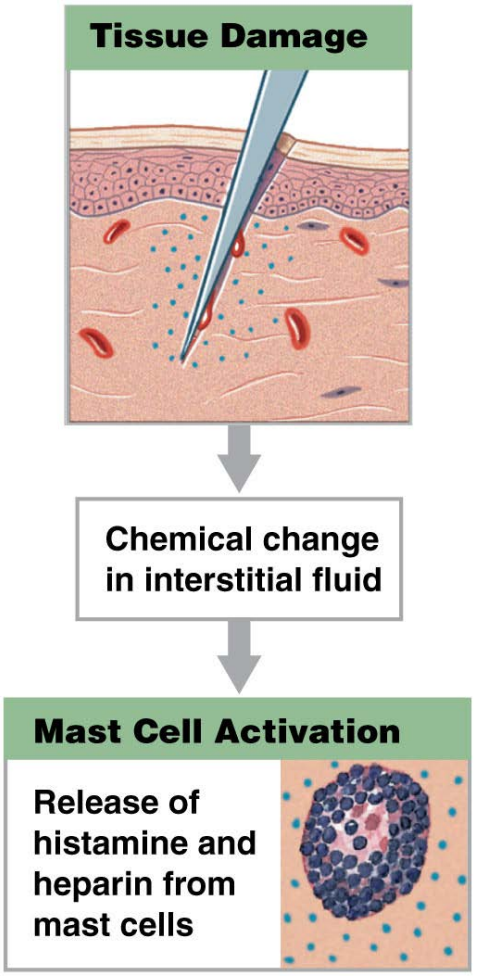
Module 20.13: Inflammation and fever

Inflammation (continued)

- Caused by various stimuli that kill cells, damage connective tissue fibers, or injure tissue
  - Cause a change in chemical composition of the interstitial fluid
    - Damaged cells release prostaglandins, proteins, and potassium ions
    - Foreign proteins or pathogens may have been introduced
  - Changes trigger complex inflammation response



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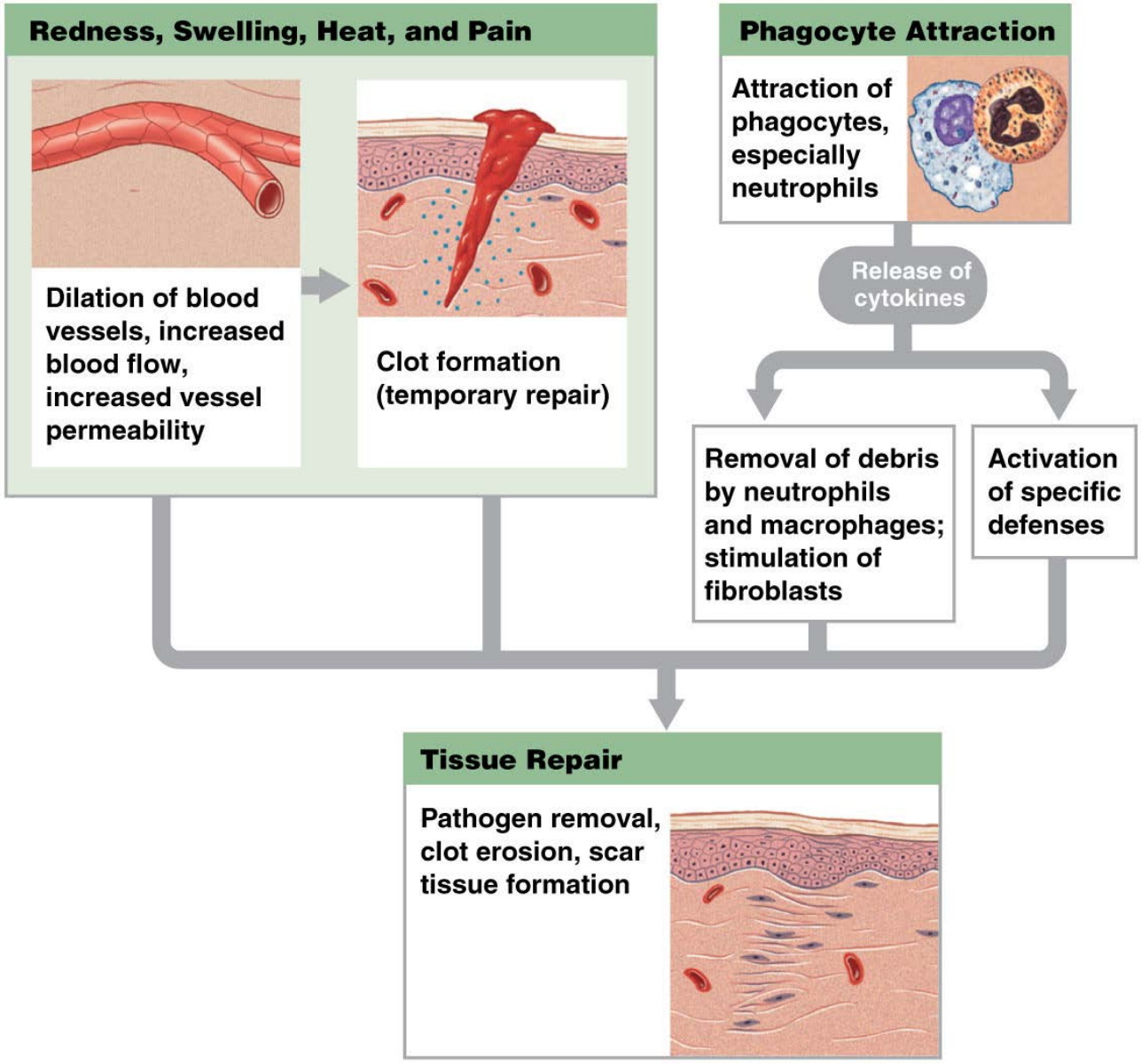
Inflammation



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Module 20.13: Inflammation and fever

Fever

- Body temperature >37.2ºC (99ºF)
- **Pyrogens** (*pyro*-, fever or heat, + *-gen,* substance)
  - Circulating fever-inducing proteins
  - Reset temperature thermostat in hypothalamus
    - Raise body temperature
- Can be beneficial within limits
  - May inhibit some viruses and bacteria
  - Increases metabolic rate, which may accelerate tissue defenses and repair process

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Module 20.13: Inflammation and fever

Summary of innate immunity

- **Physical barriers**
  - Prevent approach of pathogens and deny them access
- **Phagocytes**
  - Remove debris and pathogens
- **Immune surveillance**
  - Destroys abnormal cells
- **Interferons**
  - Increase resistance of cells to viral infections
  - Slow the spread of disease

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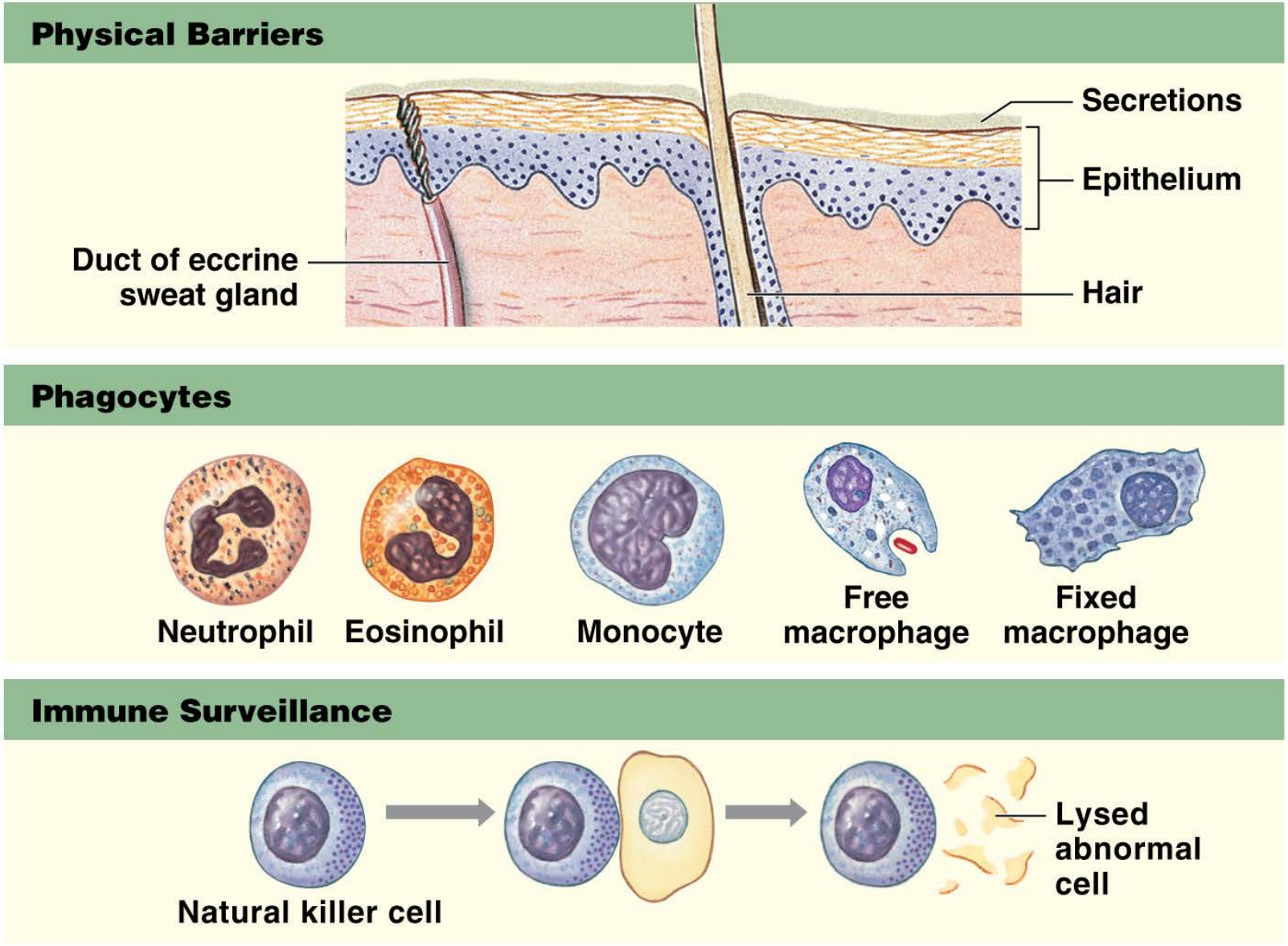
Summary of innate immunity



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Module 20.13: Inflammation and fever

Summary of innate immunity (continued)

- **Complement system**
  - Attacks and breaks down surfaces of cells, bacteria, and viruses
  - Attracts phagocytes
  - Stimulates inflammation
- **Inflammation** (multiple effects)
- **Fever**
  - Mobilizes defenses
  - Accelerates repairs
  - Inhibits pathogens

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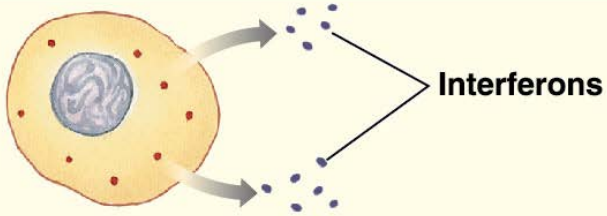
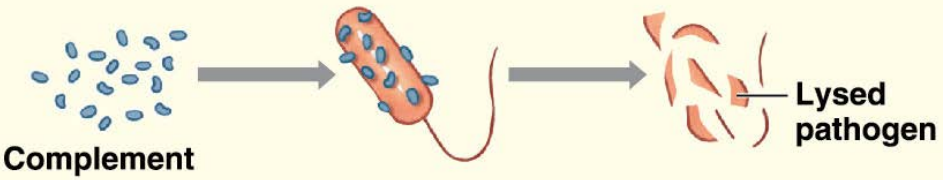
Summary of innate immunity

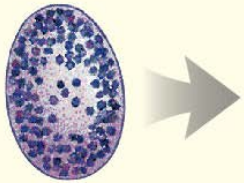
Interferons



Complement System

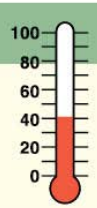


Inflammation



1. Increases blood flow
2. Activates macrophages
3. Increases capillary permeability
4. Activates complement
5. Stimulates regional clotting reaction
6. Increases regional temperature
7. Activates adaptive defenses

Fever



Body temperature rises above 37.2°C

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Module 20.13: Review

A. Describe inflammation.
B. What effect do pyrogens have in the body?
C. A rise in the level of interferons in the body suggests what kind of infection?

Learning Outcome: Explain the significance of inflammation and fever as innate defense mechanisms.

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Section 3: Adaptive immunity

Learning Outcomes

20.14 Describe the types of adaptive immunity and four properties of adaptive immunity.

20.15 Explain how antigens trigger an immune response.

20.16 Explain the events of antigen recognition and the roles of CD markers in T cell differentiation.

20.17 Explain the sensitization and activation of B cells and the role of plasma cells.

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Section 3: Adaptive immunity

Learning Outcomes (continued)

20.18 Describe the structure of an antibody, discuss the types of antibodies, and explain the primary and secondary responses to antigen exposure.

20.19 Explain the mechanisms by which antibodies destroy target antigens.

20.20 **Clinical Module:** Explain hypersensitivities, anaphylaxis, and the role of antibodies in each.

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Section 3: Adaptive immunity

Learning Outcomes (continued)

20.21 Summarize the integration of innate and adaptive immunity.

20.22 **Clinical Module:** Explain autoimmune disorders, transplant rejection, and immunodeficiency diseases, and describe age-related changes in the immune response.

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Module 20.14: Adaptive immunity provides the body's specific defenses

Adaptive (**specific**) **immunity**

- Coordinated and produced by T cells and B cells
- Not present at birth
- Acquired by
  - Exposure to antigen
    - Active immunity
  - Receiving antibodies
    - Passive immunity

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Module 20.14: Adaptive immunity

Adaptive (**specific**) **immunity** (continued)

- **Active immunity**
  - **Naturally acquired**
    - Develops after natural exposure to antigens in the environment
    - *Example:* contracting the measles gives immunity against future infection by that specific pathogen

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Module 20.14: Adaptive immunity

Adaptive (**specific**) **immunity** (continued)

- **Active immunity** (continued)
  - **Artificially induced**
    - Develops after administration of an antigen
    - *Example:* vaccination (immunization)
      - **Vaccines** contain dead or inactive pathogens, antigens derived from those pathogens, or simulated antigens
      - Stimulate immune response to produce antibodies against that specific pathogen

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Module 20.14: Adaptive immunity

Adaptive (**specific**) **immunity** (continued)

- **Passive immunity**
  - **Naturally acquired**
    - *Example*: transfer of maternal antibodies across placenta or breast milk
  - **Artificially induced**
    - *Example*: administration of antibodies to a patient

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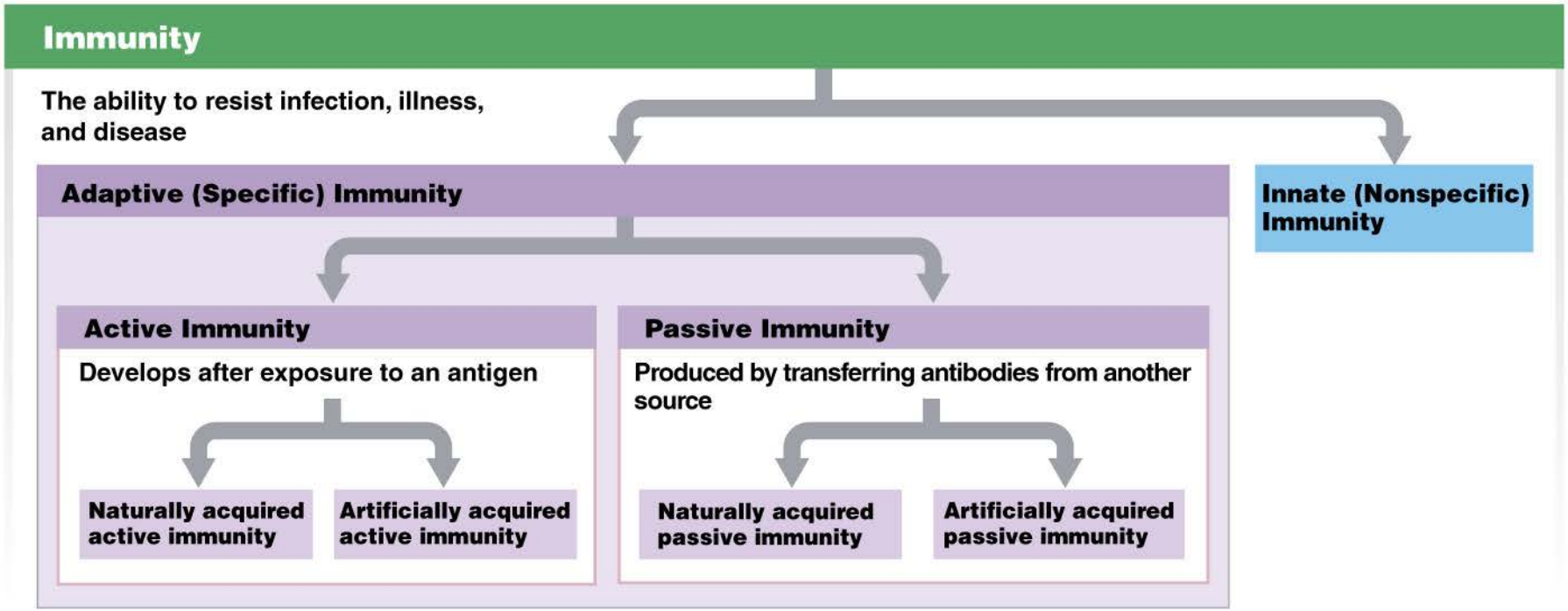
Adaptive immunity



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Module 20.14: Adaptive immunity

Properties of adaptive immunity

1. **Specificity**
   - T cells and B cells have receptors for only one specific antigen
   - Responses of activated T cell or B cell are also specific (do not affect any other antigens)
2. **Versatility**
   - Millions of lymphocytes, each sensitive to a different antigen
   - When activated, a lymphocyte divides
     - Produces more lymphocytes with same specificity
     - All cells produced by the division of an activated lymphocyte constitute a **clone**

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Module 20.14: Adaptive immunity

Properties of adaptive immunity (continued)

3. **Memory**
   - Activated lymphocytes produce two groups of cells
     - Groups that attack invaders immediately
     - Group that remains inactive unless exposed to the same antigen later
       - These **memory cells** "remember" antigens, making future attacks faster, stronger, and longer lasting

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Module 20.14: Adaptive immunity

Properties of adaptive immunity (continued)

4. **Tolerance**
   - Immune response ignores “self” but targets abnormal and foreign “nonself” cells and toxins
   - Can develop over time in response to chronic exposure to an antigen

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Module 20.14: Review

A. Which two cells coordinate adaptive immunity?
B. Which type of immunity develops when a child is given the polio vaccine?

Learning Outcome: Describe the types of adaptive immunity and four properties of adaptive immunity.

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Module 20.15: Adaptive immunity is triggered by exposure of T cells and B cells to specific antigens

Overview of the immune response

- Antigens either infect cells or are “processed” by phagocytes
  - Antigens or antigenic fragments are then displayed on the plasma membrane
  - Called **antigenic presentation**
  - Triggers an immune response
- Presentation of specific antigens stimulates:
  1. Cell-mediated immunity (T cells)
  2. Antibody-mediated immunity (B cells)

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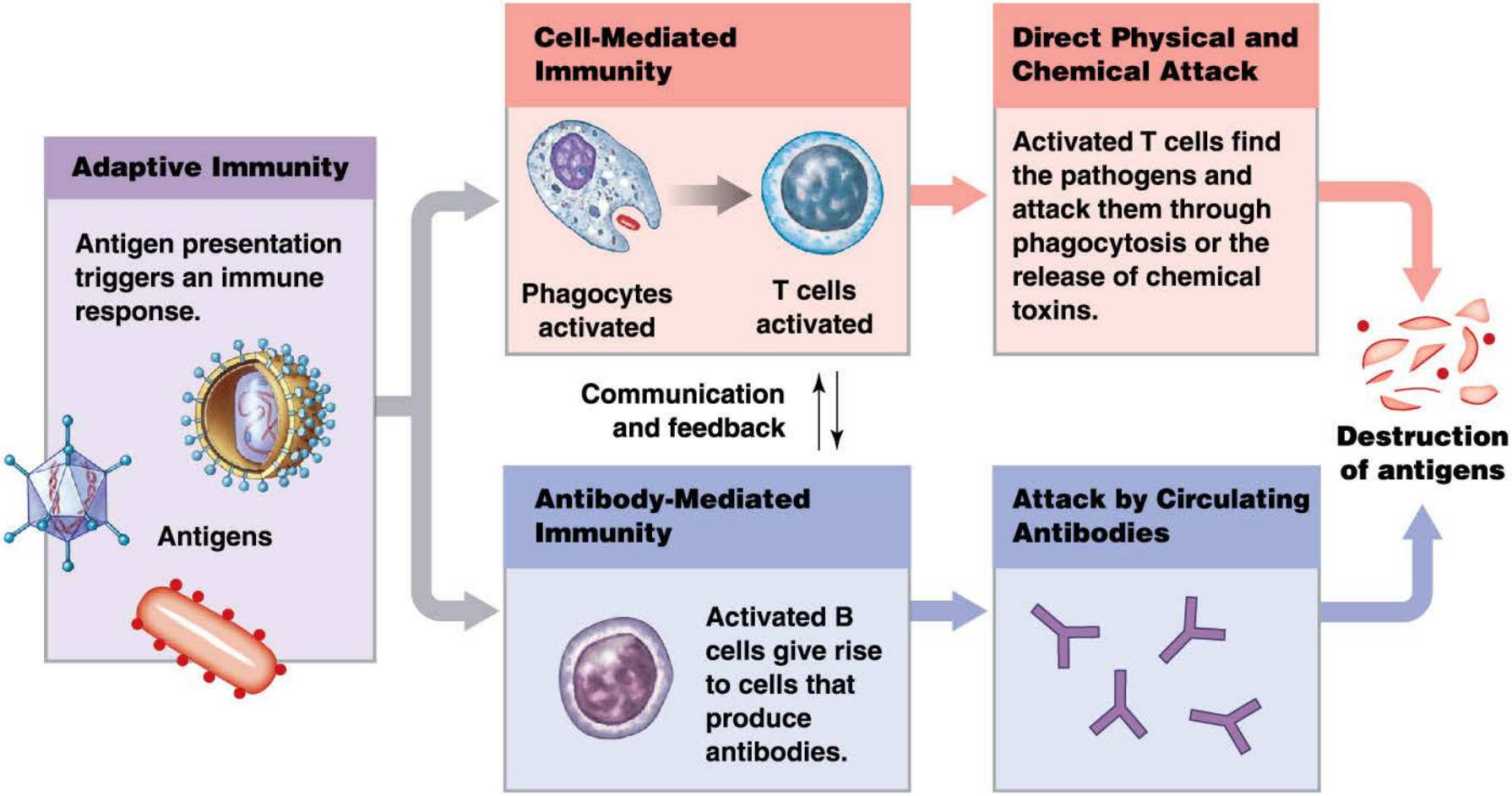
Adaptive immunity



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Module 20.15: Triggering Adaptive Immunity

Major histocompatibility complex (MHC) proteins

- Genetically determined membrane glycoproteins
  - **Major histocompatibility complex**
    - Region on chromosome 6 containing genes that control synthesis of MHC proteins
- Placement of the antigen-glycoprotein combination on the plasma membrane is called **antigen presentation**
  - Capable of activating T cells

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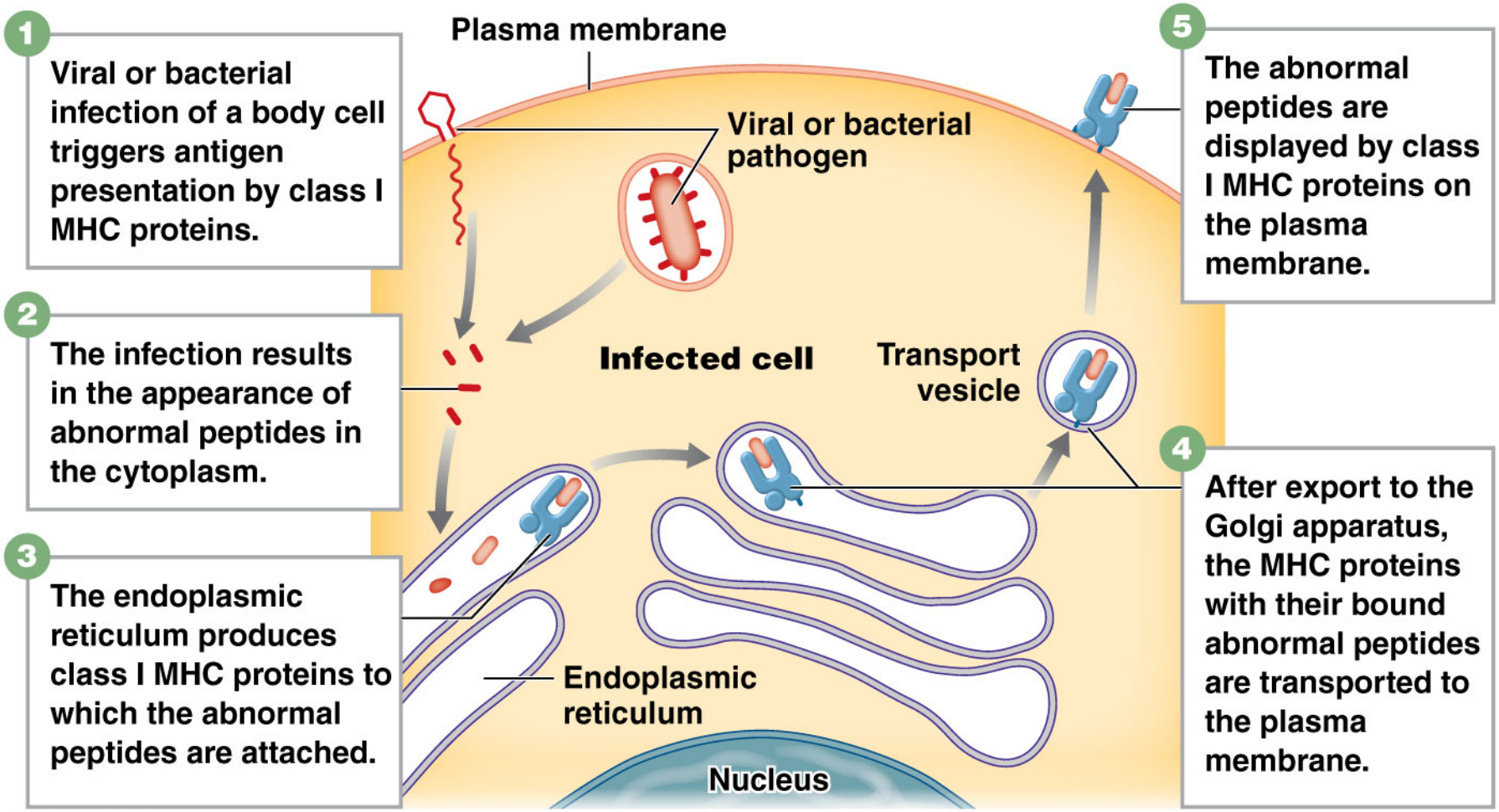
Antigen presentation with class I MHC



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Module 20.15: Triggering adaptive immunity

Classes of MHC proteins

1. **Class I MHC proteins**
   - Present in membranes of all nucleated cells
   - Triggered by viral or bacterial infection of a body cell
2. **Class II MHC proteins**
   - Present only in membranes of **antigen-presenting cells** (**APCs**)
     - *Examples*: monocyte–macrophages, dendritic cells
   - Appear only when the cell is processing antigens

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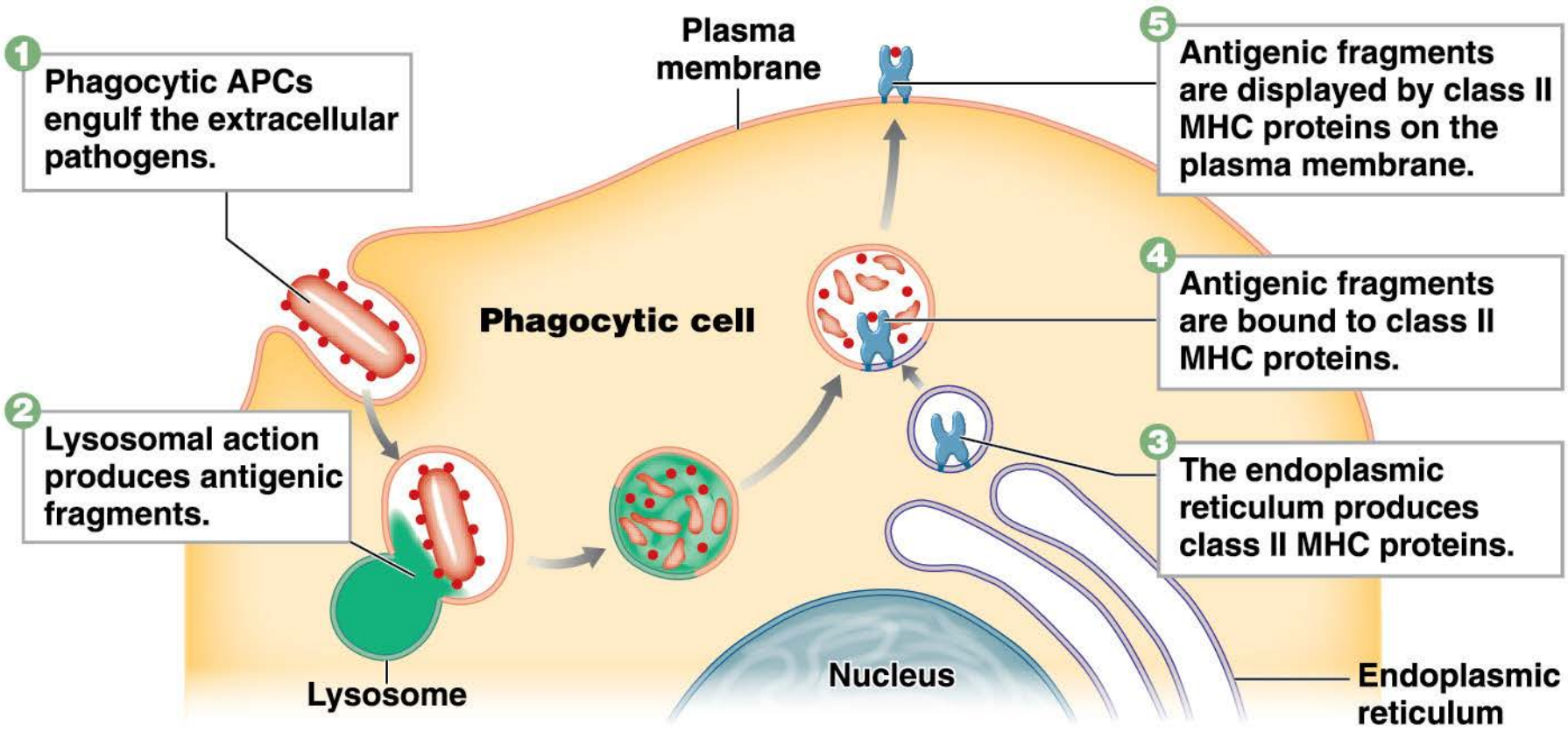
Antigen presentation with class II MHC



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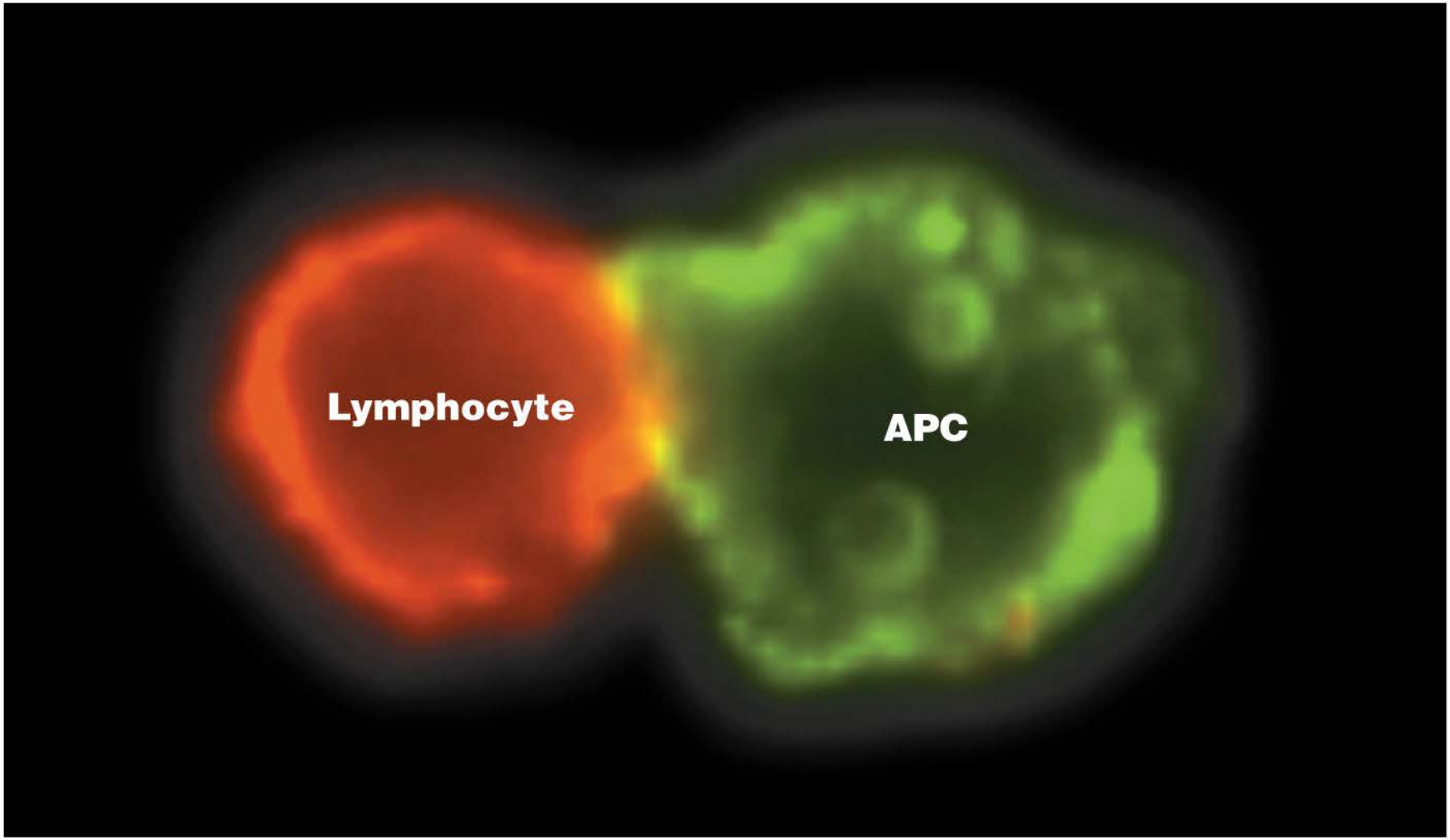
Antigen presentation with MHC proteins



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Module 20.15: Review

A. Describe antigen presentation.
B. What is the major histocompatibility complex (MHC)?
C. Where are class I MHC proteins and class II MHC proteins found?
D. What types of immunity are stimulated by antigen presentation?

Learning Outcome: Explain how antigens trigger an immune response.

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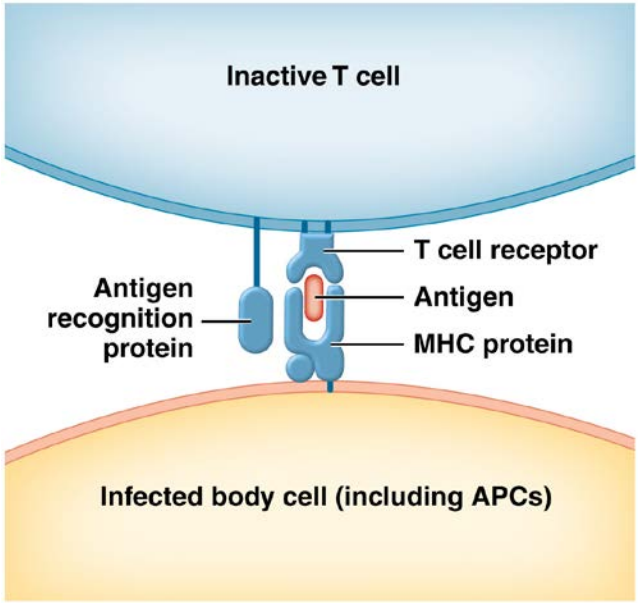
Module 20.16: Infected cells stimulate the formation and division of cytotoxic T cells, memory T_c cells, and regulatory T cells

Antigen recognition

- Inactive T cell binding to a specific MHC-antigen complex
- Inactive T cells have receptors that recognize either class I or class II MHC proteins when they are bound to specific antigens
- T cell will bind only to a complex containing the antigen that T cell is programmed to detect



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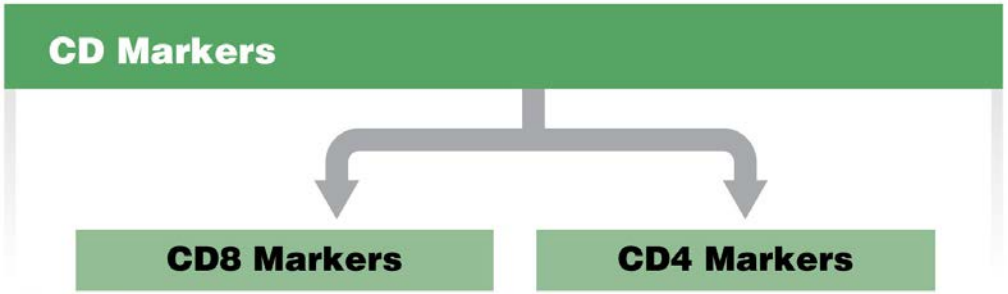
Module 20.16: Activation of T cells by infected cells

CD markers



- Membrane proteins involved in antigen recognition
- CD stands for “cluster of differentiation”
- Two classes associated with T cell
  1. **CD8 markers** (on **CD8 T cells**: cytotoxic and regulatory T cells)
     - Respond to class I MHC proteins
  2. **CD4 markers** (on **CD4 T cells**: helper T cells)
     - Respond to class II MHC proteins

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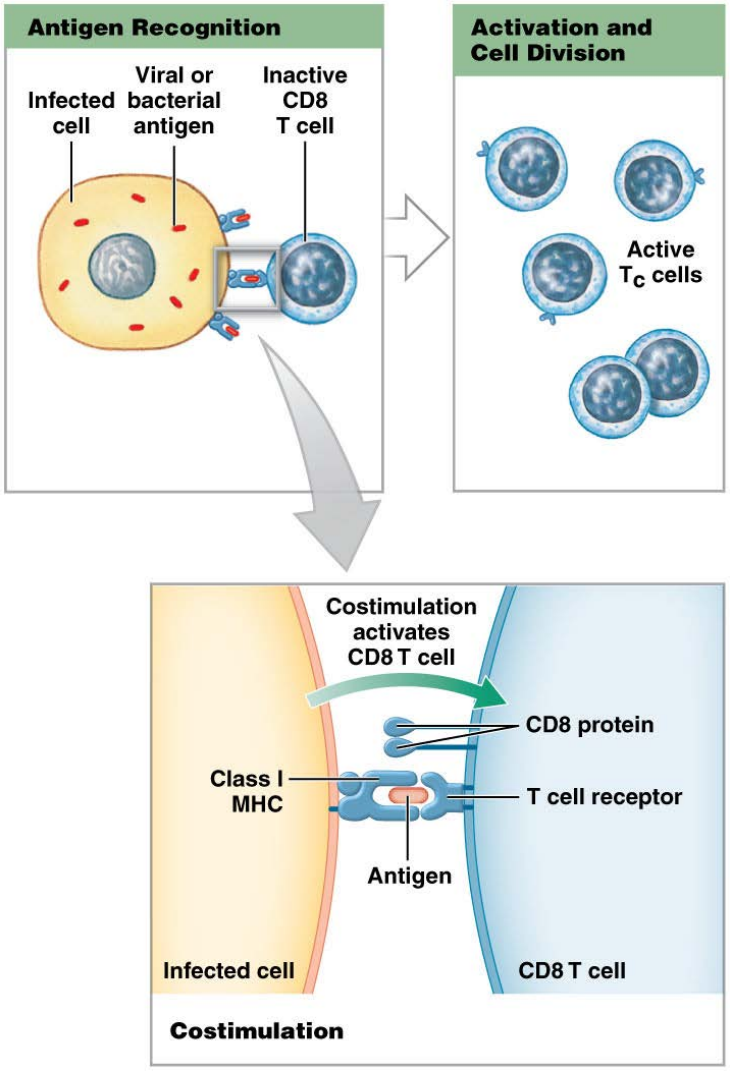
Module 20.16: Activation of T cells by infected cells

Activation of CD8 T cells

1. **Antigen recognition**
   - Occurs when CD8 T cell encounters specific antigen bound to a class I MHC protein on the surface of another cell



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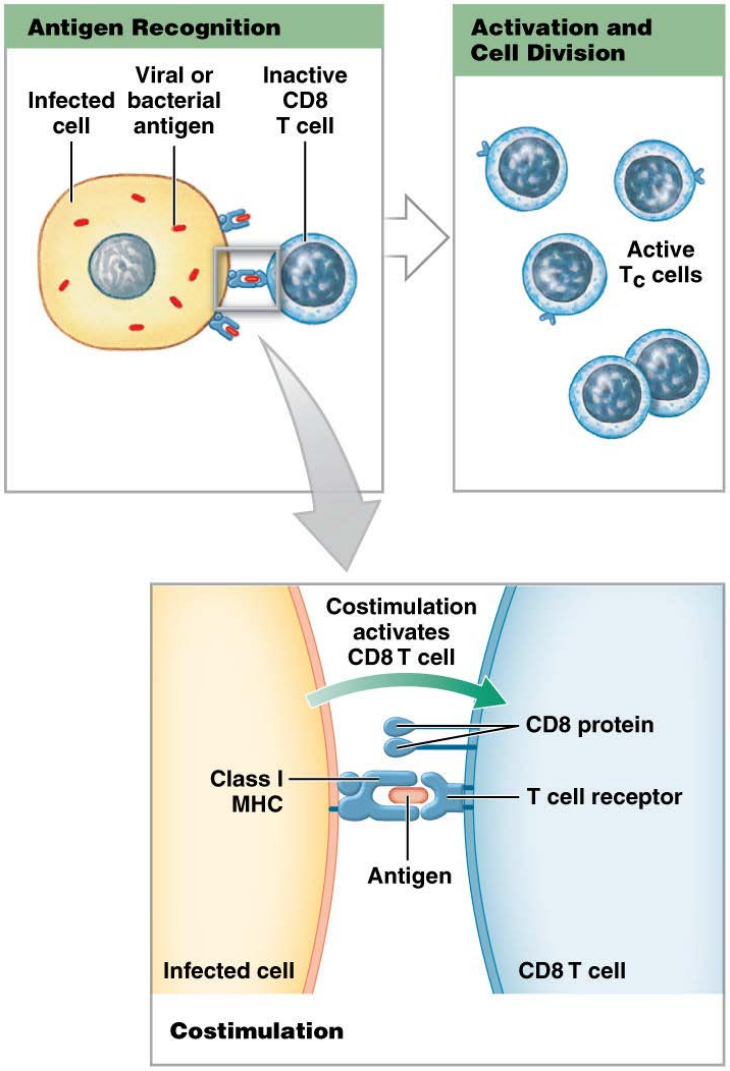
Module 20.16: Activation of T cells by infected cells

Activation of CD8 T cells (continued)

2. **Costimulation**
   - Physical or chemical stimulation of T cell in addition to the class I MHC molecule
   - Like the safety on a gun: prevents T cells from mistakenly attacking normal cells



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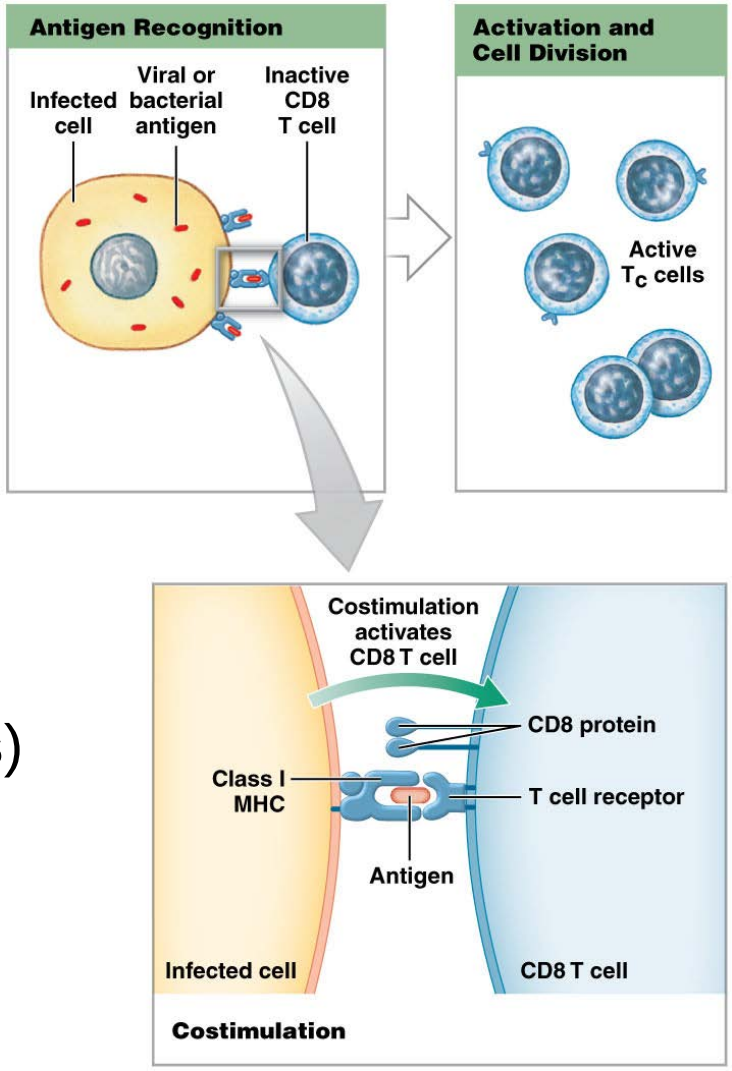
Module 20.16: Activation of T cells by infected cells

Activation of CD8 T cells (continued)

3. **Activation and cell division**
   - Three different types of CD8 T cells produced (all sensitive to the same antigen)
     1. **Cytotoxic T cells (T_C cells)**
     2. **Memory T_C cells**
     3. **Regulatory T cells (T_{reg} cells)**



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Module 20.16: Activation of T cells by infected cells

CD8 T cell types

1. **Cytotoxic T cells (T_C cells)**
   - Seek out and destroy abnormal and infected cells
     - Target cells must have specific class I MHC proteins
     - Destructive mechanisms
       - Release of perforins
       - Activation of self-destruction genes of target cell for cell death (**apoptosis**)
       - Disruption of cell metabolism with **lymphotoxin**

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Module 20.16: Activation of T cells by infected cells

CD8 T cell types (continued)

2. **Memory T_C cells**
   - Are produced but do not differentiate further during first antigen exposure
   - Upon second exposure to same antigen, memory T_C cells become cytotoxic T cells
3. **Regulatory T cells**
   - Secrete **suppression factors** to limit responses of other T cells and B cells
   - Also act only after first antigen exposure (initial immune response)

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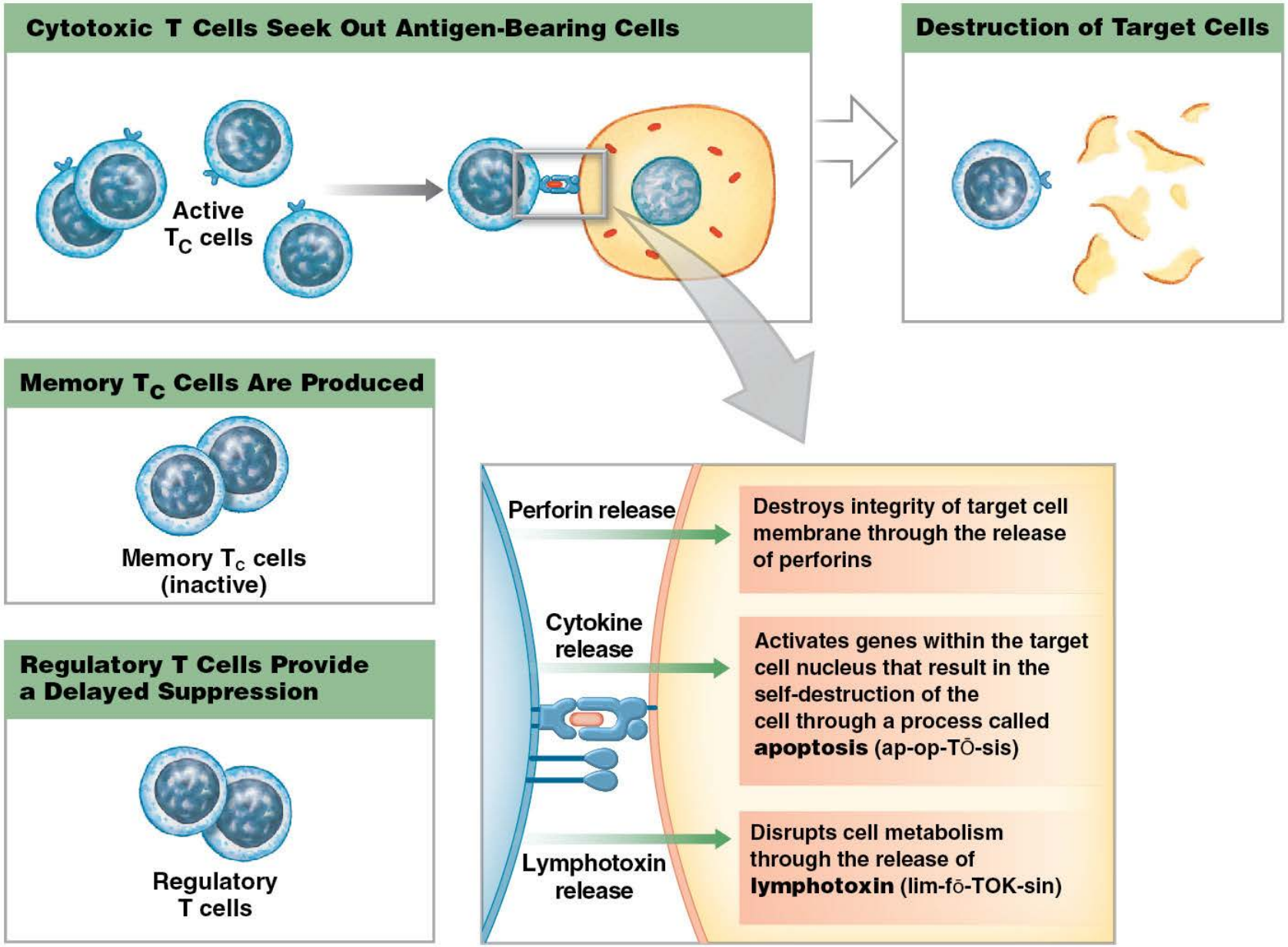
Differentiation of CD8 T cells



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Module 20.16: Review

A. Describe CD markers.
B. Identify the three major types of T cells activated by class I MHC proteins.
C. How do abnormal antigens attached to class I MHC proteins initiate an immune response?

Learning Outcome: Explain the events of antigen recognition and the roles of CD markers in T cell differentiation.

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Module 20.17: Antigen-presenting cells can stimulate activation of CD4 T cells, producing helper T cells that promote B cell activation and antibody production

Activation of CD4 T cells

- First must be exposed to antigens bound to class II MHC proteins
- Costimulation completes activation
- Next step involves series of divisions
  - Daughter cells differentiate into active **helper T cells** (**T_H cells**) and **memory T_H cells**
- Active helper T cells secrete **cytokines**
  - Stimulate both cell-mediated and antibody-mediated immunity

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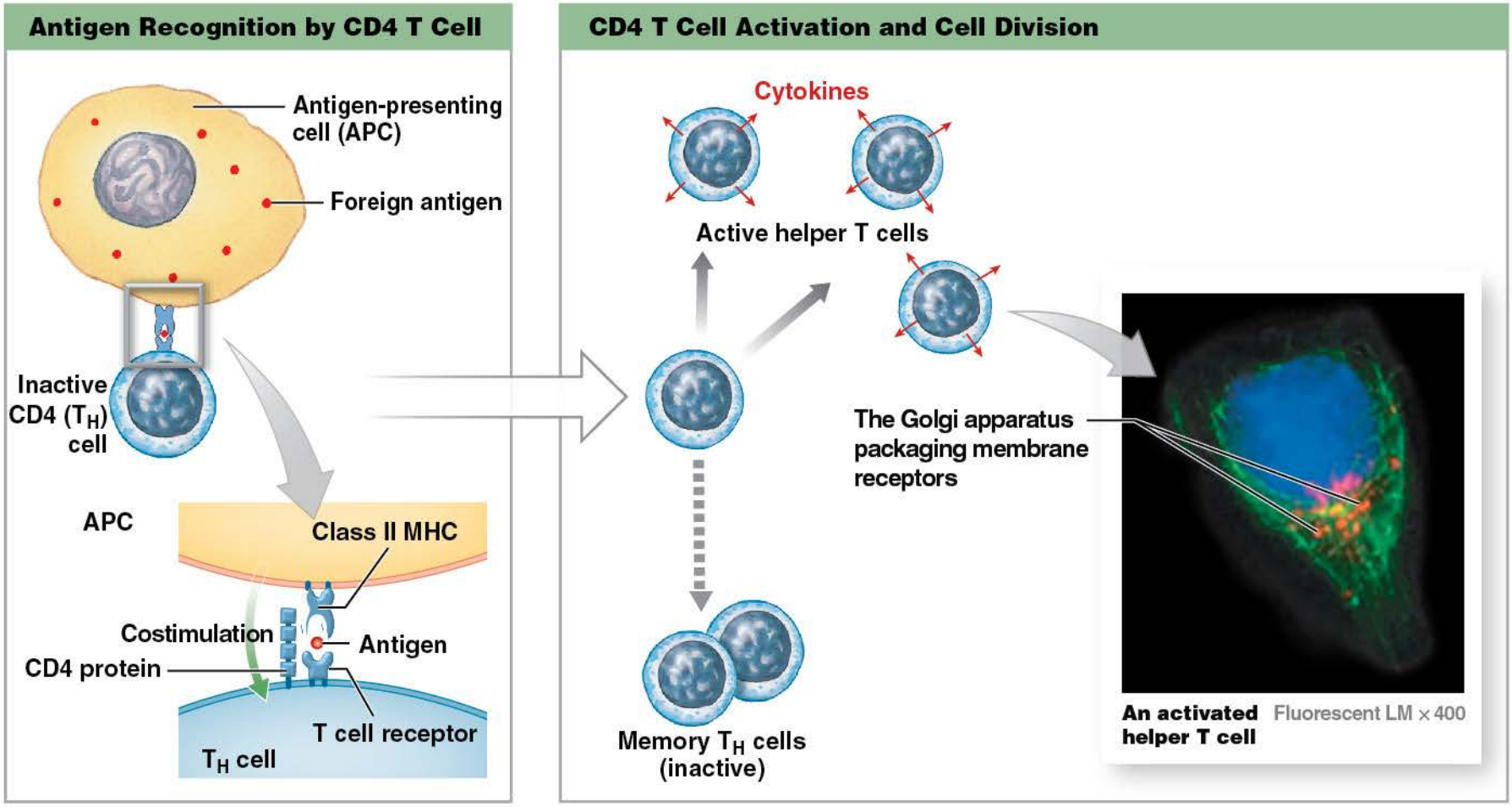
Activation of CD4 T cell activation



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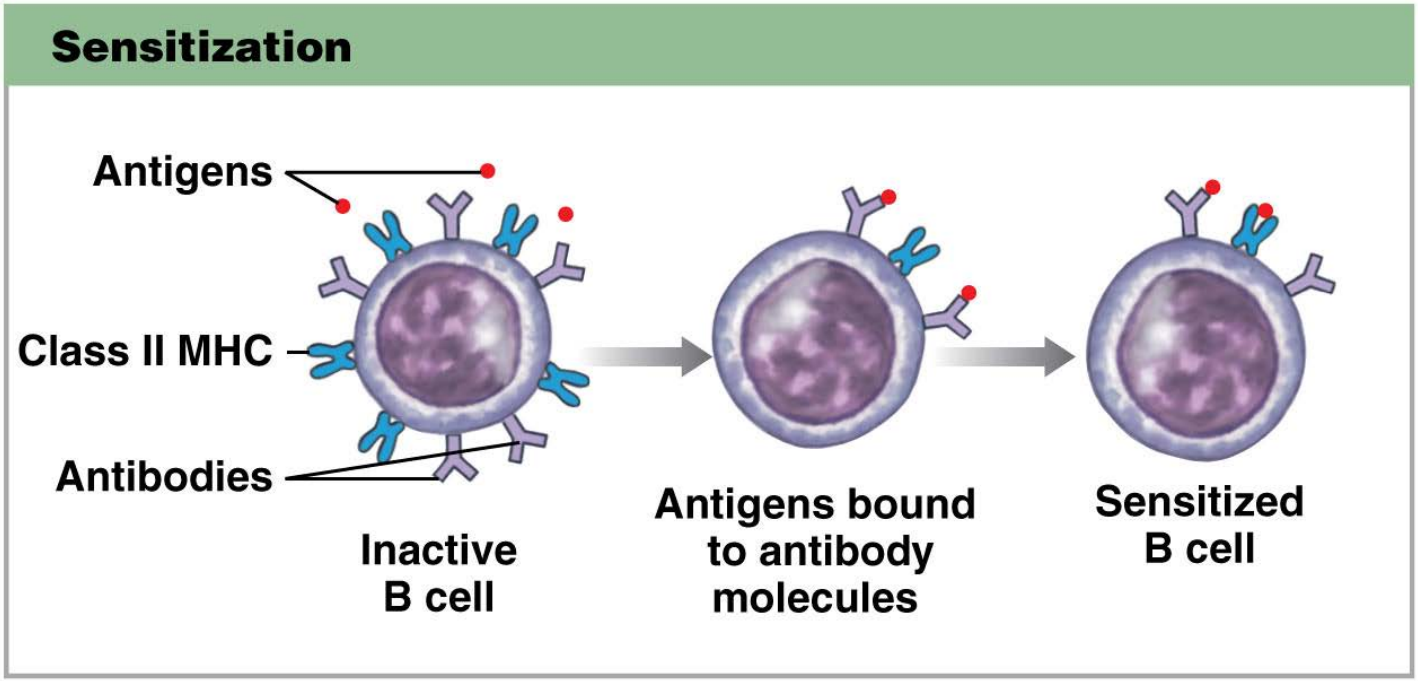
Module 20.17: CD4 T cell and B cell activation

B cell sensitization

- Preparation for activation is called **sensitization**
  - Antigens are brought into cell through endocytosis and then placed on surface of cell bound to class II MHC proteins



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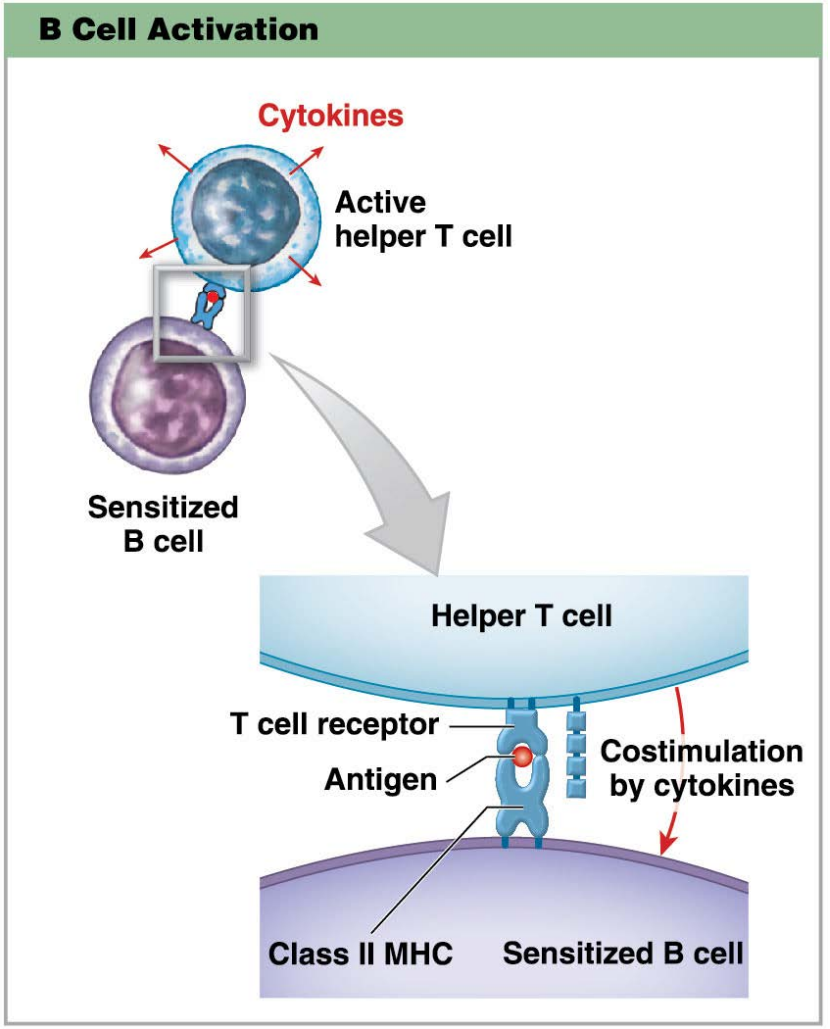
Module 20.17: CD4 T cell and B cell activation

B cell activation

- Full activation requires helper T cell
  - Helper T cell must have been activated by exposure to the same antigen
  - Helper T cell binds to MHC complex of sensitized B cell
    - Secretes cytokines to promote B cell activation



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Module 20.17: CD4 T cell and B cell activation

B cell division, differentiation, and antibody production

- Stimulation by cytokines causes series of cell divisions in B cells
- Two types of daughter cells
  - **Memory B cells**
    - Inactive until second exposure to antigen
    - Respond then by differentiating into plasma cells
  - **Plasma cells**
    - Activated B cells, each capable of secreting up to 100 million antibody molecules per hour

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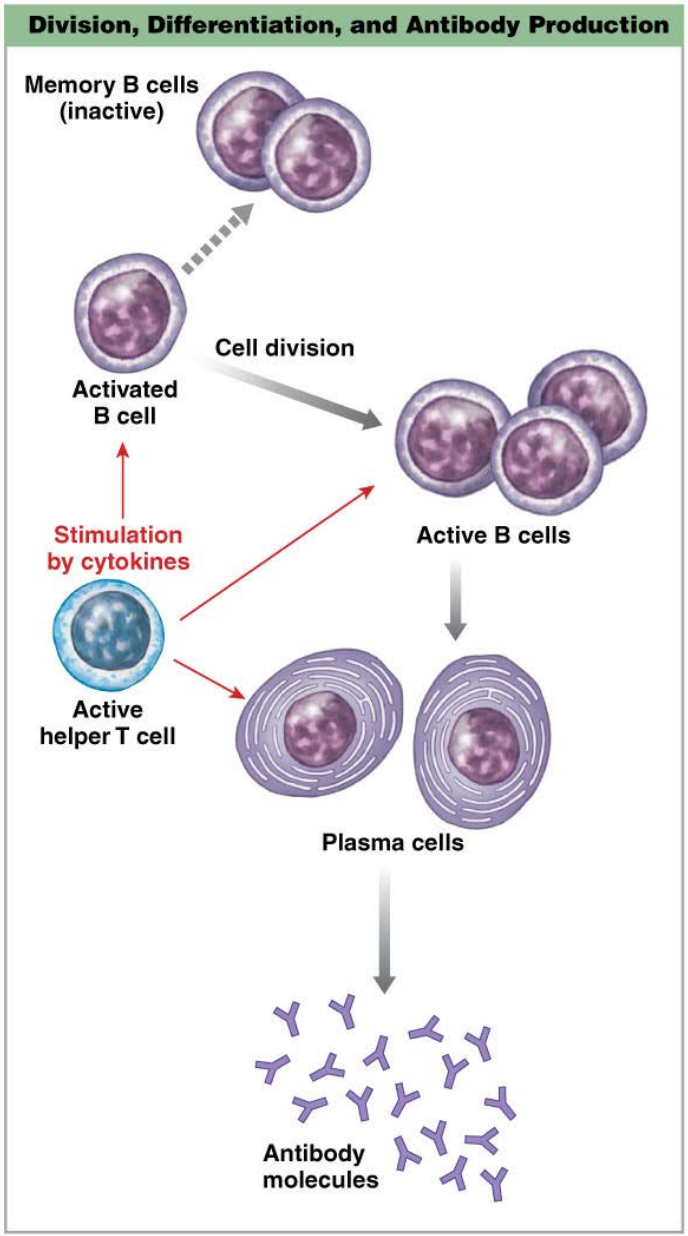
B cell division, differentiation, and antibody production



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Module 20.17: Review

A. Explain the function of cytokines secreted by helper T cells.
B. Define *sensitization*.
C. If you observed a higher-than-normal number of plasma cells in a sample of lymph, would you expect antibody levels in the blood to be higher or lower than normal?

Learning Outcome: Explain the sensitization and activation of B cells and the role of plasma cells.

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Module 20.18: Antibodies are small soluble proteins that bind to specific antigens and whose abundance increases upon later antigen exposure

Molecule structure

- Consists of two parallel polypeptide chains
  - One pair of **heavy chains**
  - One pair of **light chains**
- Each pair contains:
  - **Constant segments**
    - On heavy chains, form the base of antibody molecule
  - **Variable segments**
    - Free tips are **antigen binding sites**
    - Differences in amino acid sequences produce variability needed for different antibodies

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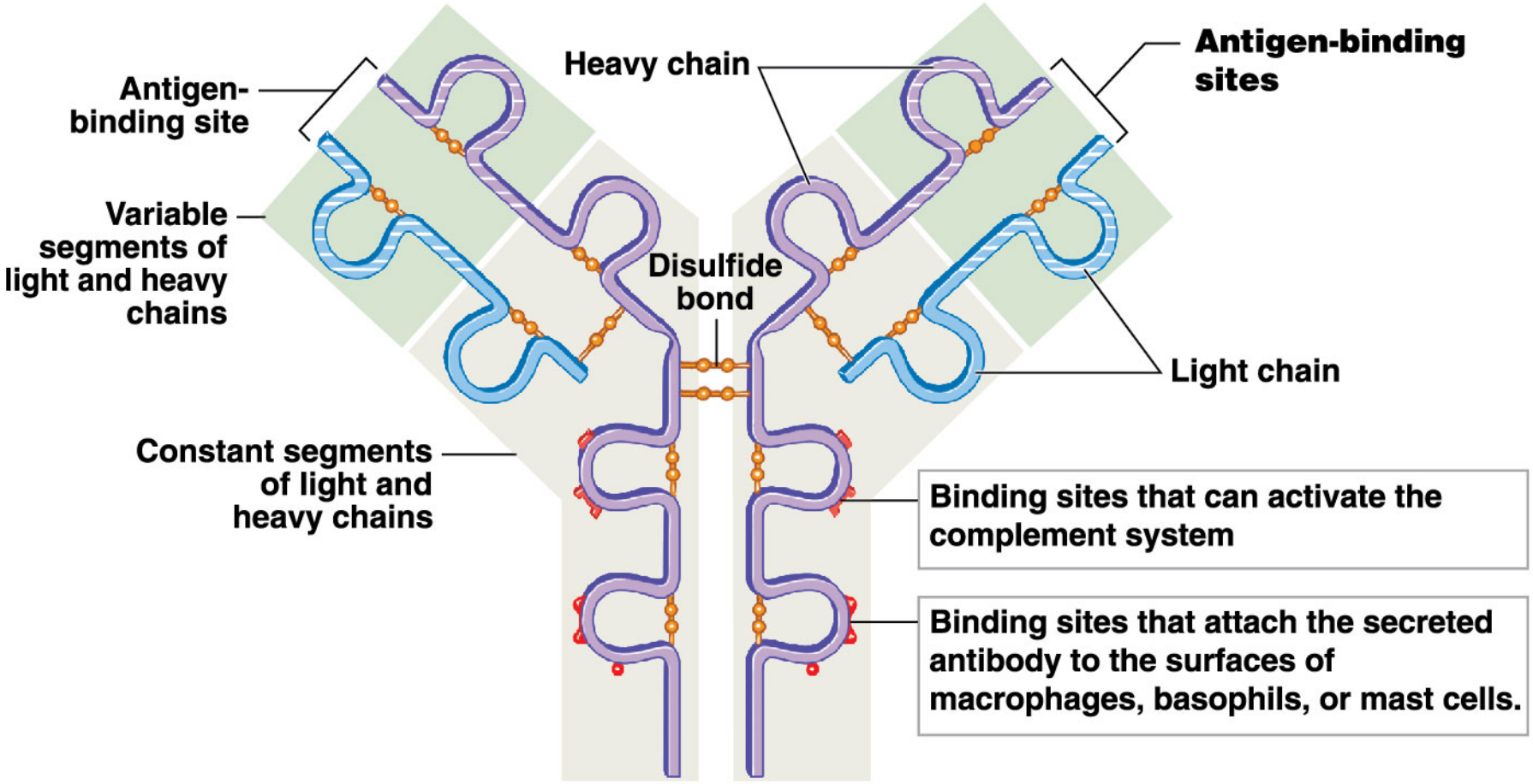
Antibody structure



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Module 20.18: Antibodies

Antigen-antibody complex

- Formed when a specific antibody molecule binds to its corresponding antigen molecule
  - Binds to specific portions of the exposed surface called **antigenic determinant sites** on an antigen
- Bacteria may contain millions of antigenic determinant sites

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Module 20.18: Antibodies

Types of antigens

- **Complete antigens**
  - Have at least two antigenic determinant sites, one for each binding site on antibody
- **Hapten** (partial antigens)
  - Do not ordinarily cause B cell activation
  - Can attach to carrier molecules and function as a complete antigen
  - Antibodies will attack both hapten and carrier molecule
    - If carrier molecule is normally found in tissues, antibodies may attack normal cells
    - Basis for drug reactions, such as allergies to penicillin

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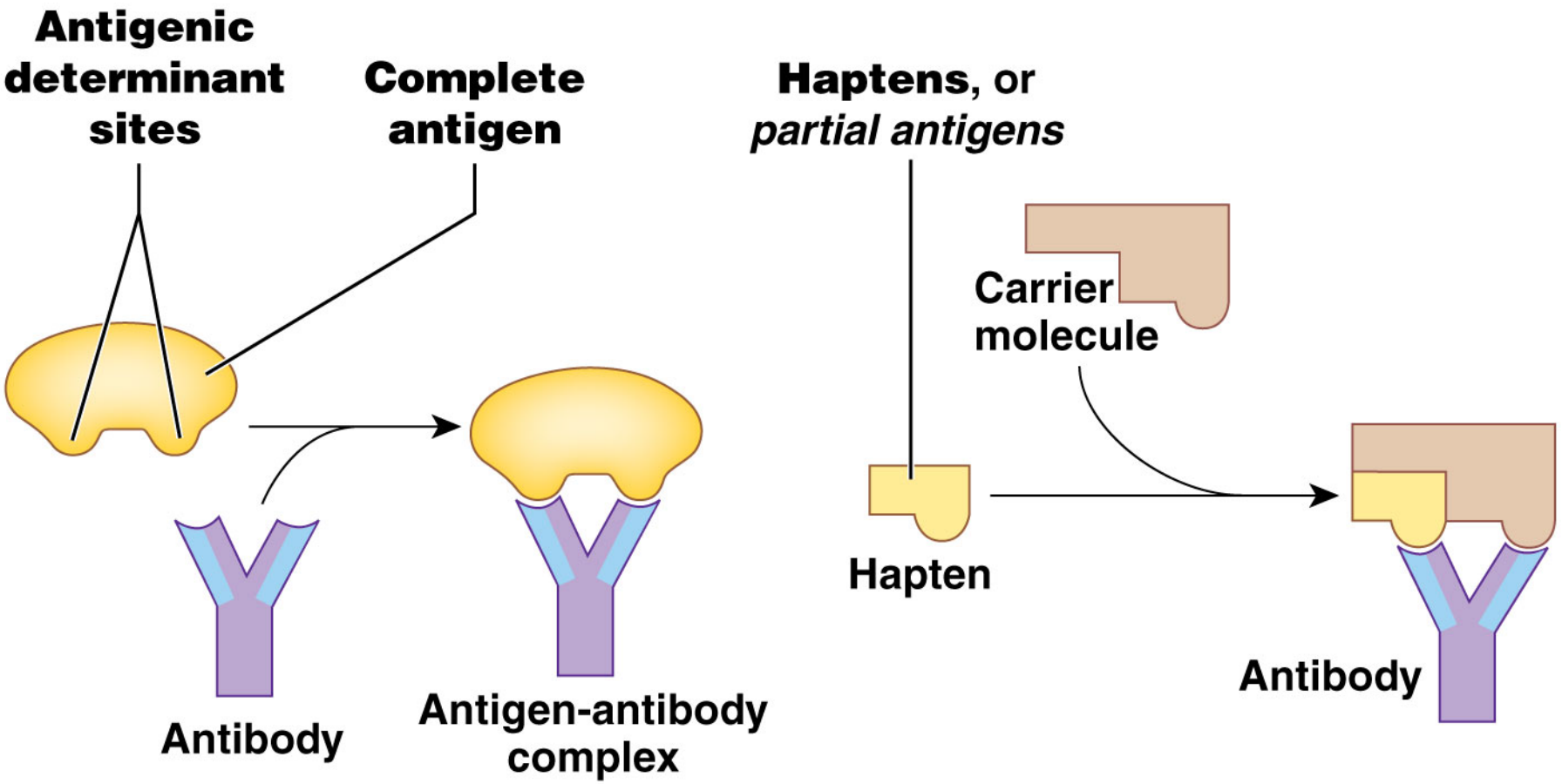
Antigen-antibody complex



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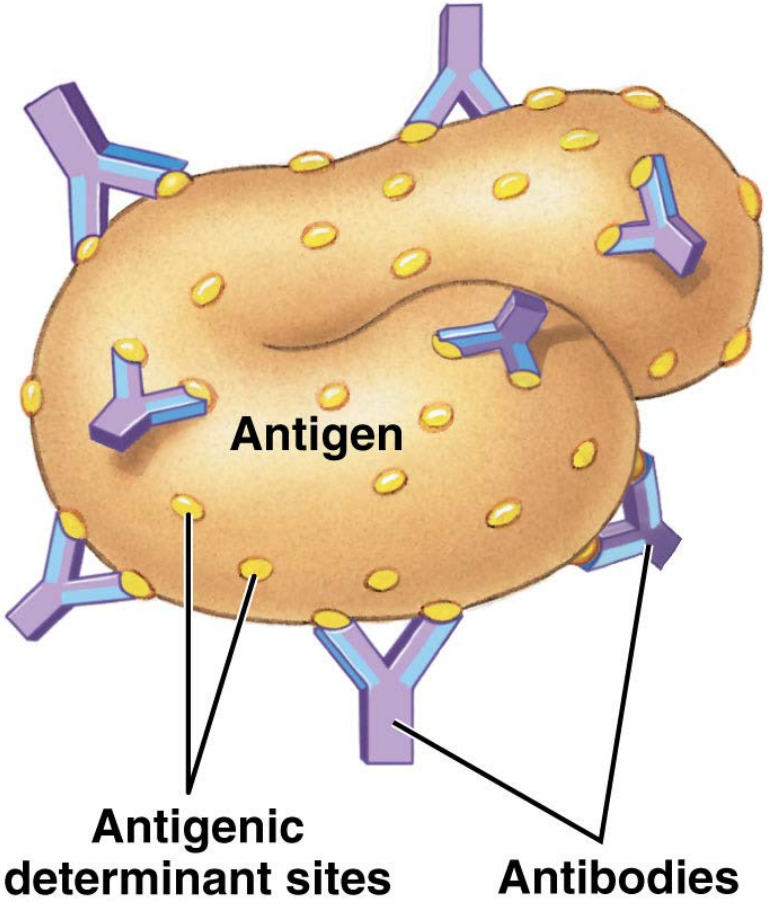
Module 20.18: Antibodies

A bacterium can contain millions of antigenic determinant sites

- Can become carpeted with antibodies



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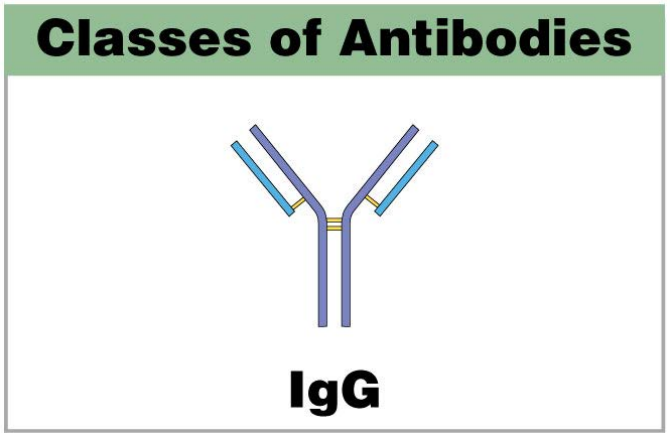
Module 20.18: Antibodies

Classes of antibodies, or immunoglobulins (Igs)

- Class determined by differences in structure of the heavy-chain constant segments



1. **IgG** (80 percent of all antibodies)
   - Responsible for resistance against many viruses, bacteria, and bacterial toxins

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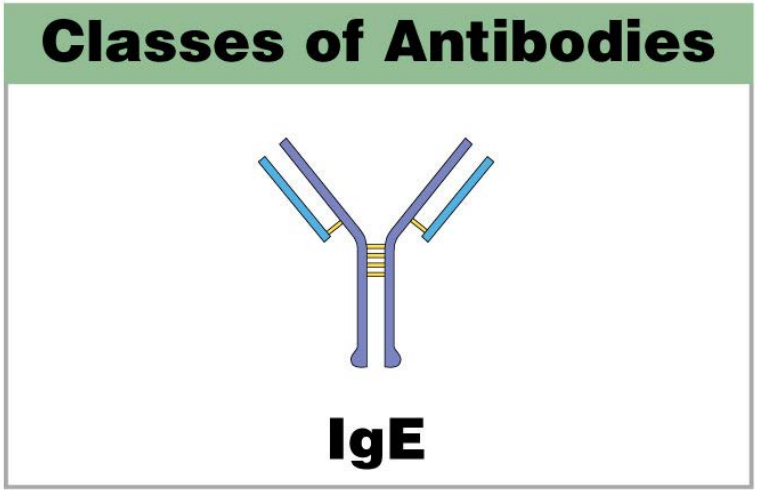
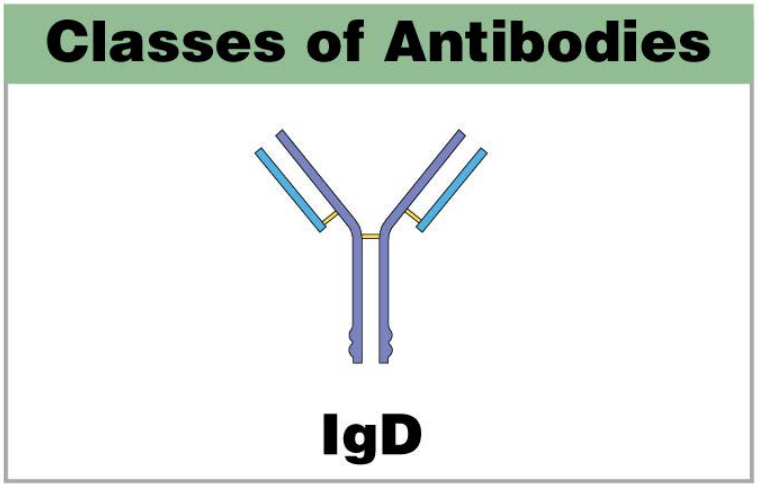
Module 20.18: Antibodies

Classes of antibodies (continued)

2. **IgE**
   - Attaches to basophil and mast cell surfaces
3. **IgD**
   - On B cell surface, where it binds antigens in extracellular fluid
   - Plays role in B cell sensitization





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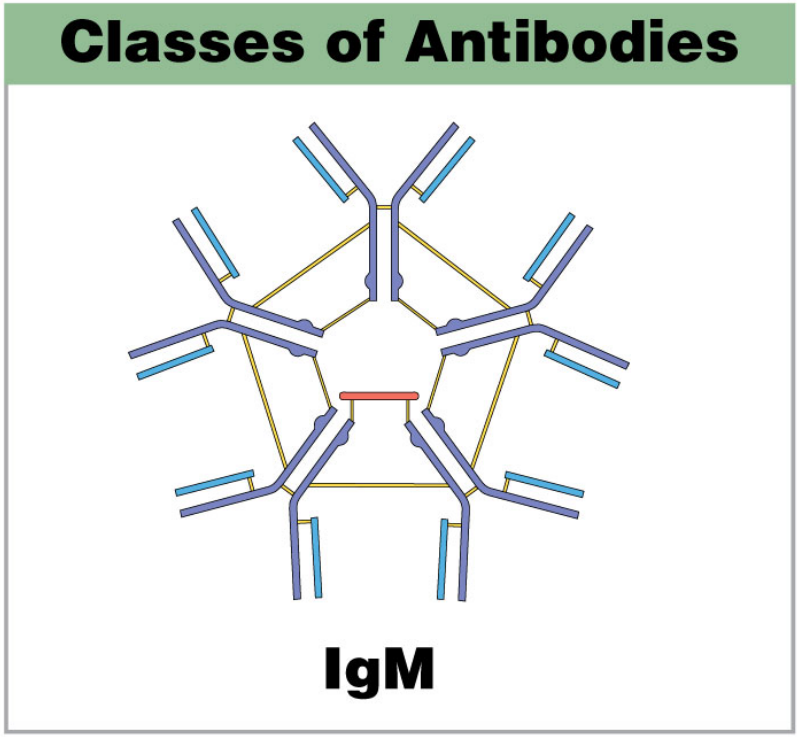
Module 20.18: Antibodies

Classes of antibodies (continued)

4. **IgM**
   - First class of antibody secreted after antigen encountered
     - Production declines as IgG production increases
   - Anti-A and anti-B antibodies are examples



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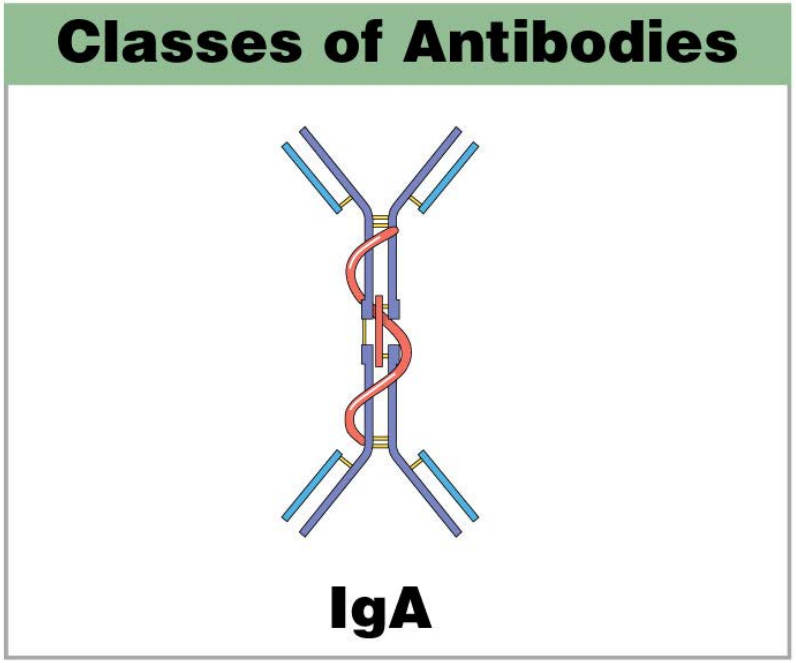
Module 20.18: Antibodies

Classes of antibodies (continued)

5. **IgA**
   - Found primarily in glandular secretions, such as mucus, tears, saliva, and semen
   - Attack before pathogens gain internal access



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Module 20.18: Antibodies

Responses to antigen exposure

- **Primary response**
  - Antibody-mediated response to initial antigen exposure
  - Takes time to develop
    - Appropriate B cells must be activated then differentiate into antibody-secreting plasma cells
  - **Antibody titer** (level of antibodies in the blood) peaks 1–2 weeks after initial exposure
  - Levels decline if no longer exposed to the antigen

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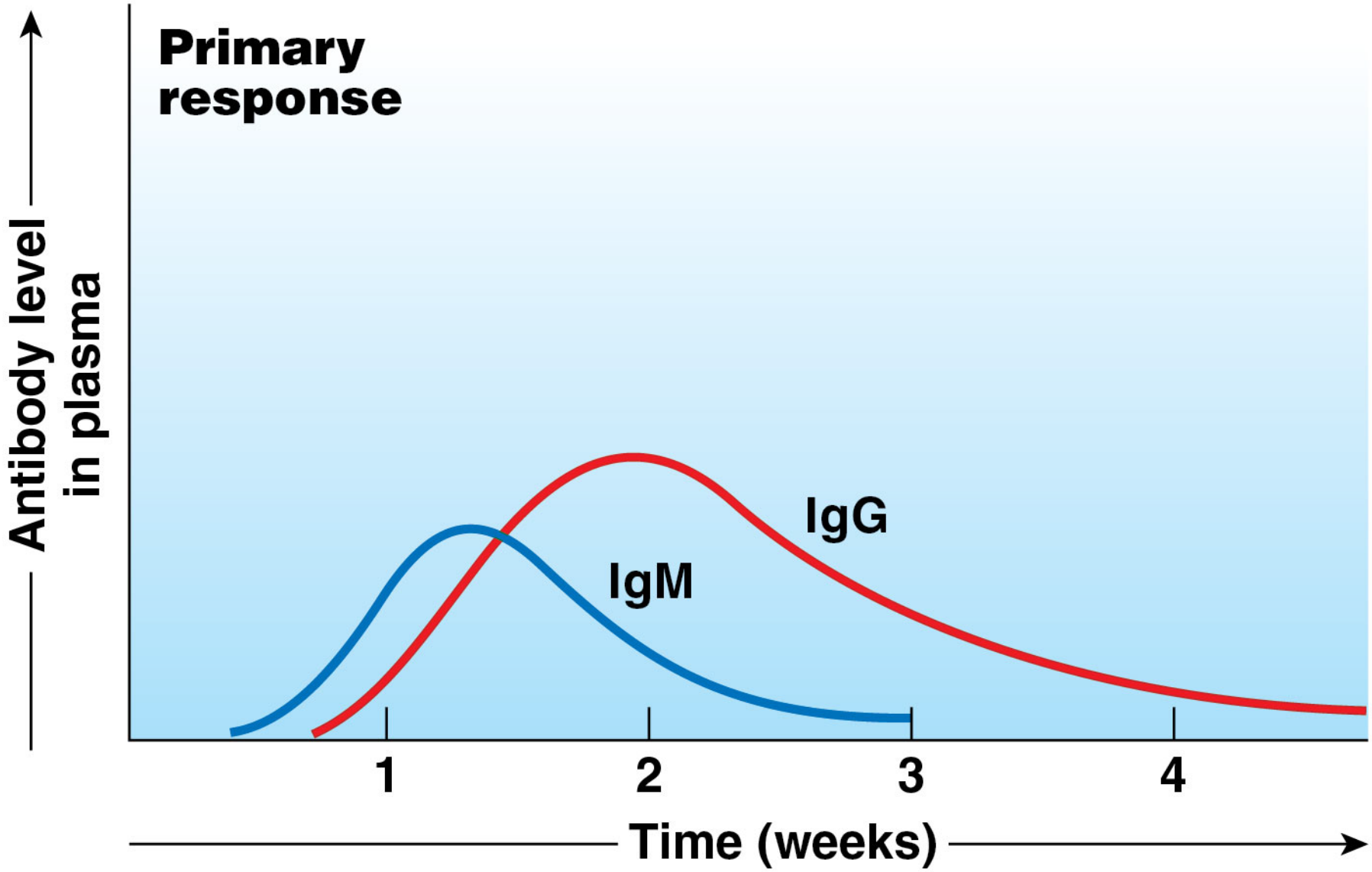
Primary response



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Module 20.18: Antibodies

Responses to antigen exposure (continued)

- **Secondary response**
  - Triggered when antigen is encountered again
  - More extensive and lasts longer than primary response
    - Antibody titers increase more rapidly and reach higher concentrations
  - Result of immediate response by memory B cells for specific antigen
  - Appears even if second exposure is years after the first
    - Memory cells may survive 20 years or more

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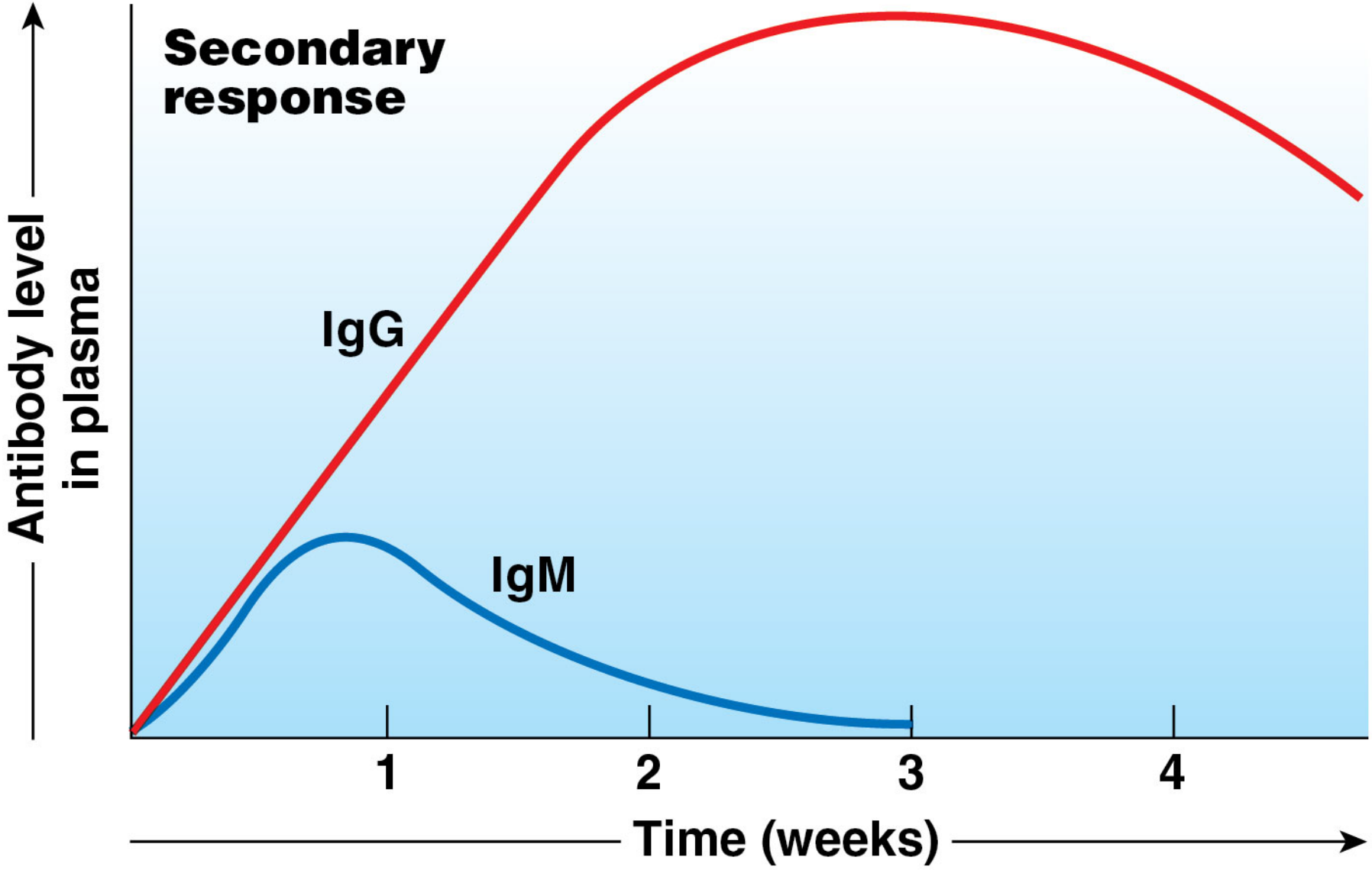
Secondary response



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Module 20.18: Review

A. Describe the structure of an antibody.
B. Define *antigenic determinant site*.
C. Which would be more affected by a lack of memory B cells and memory T cells: the primary response or the secondary response?

Learning Outcome: Describe the structure of an antibody, discuss the types of antibodies, and explain the primary and secondary responses to antigen exposure.

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Module 20.19: Antibodies use many different mechanisms to destroy target antigens

Methods of eliminating antigens

1. **Neutralization**
   - Antibodies occupy binding sites on viruses and bacterial toxins, preventing them from affecting body cells
2. **Prevention of pathogen adhesion**
   - IgA antibodies in glandular secretions cover bacteria or viruses, preventing adhesion and infection of body cells
3. **Activation of complement**
   - After antigen binding, complement also can bind to the antibody, accelerating the complement cascade

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Module 20.19: Antibody mechanisms

Methods of eliminating antigens (continued)

4. **Stimulation of inflammation**
   - Stimulate basophil and mast cells to release chemicals
5. **Opsonization**
   - Coating of pathogen with antibodies allows phagocytes to bind more easily
6. **Attraction of phagocytes**
   - Attached antibodies attract eosinophils, neutrophils, and macrophages

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Module 20.19: Antibody mechanisms

Methods of eliminating antigens (continued)

7. **Precipitation and agglutination**
   - Antibodies can bind to antigenic determinant sites on adjacent antigens
   - The linking of multiple pathogens by antibodies creates an **immune complex**
     - Formation of insoluble complexes (too large to stay in solution) is called **precipitation**
     - Formation of an immune complex from surface antigens is called **agglutination**
       - *Example:* clumping of RBCs in a transfusion reaction

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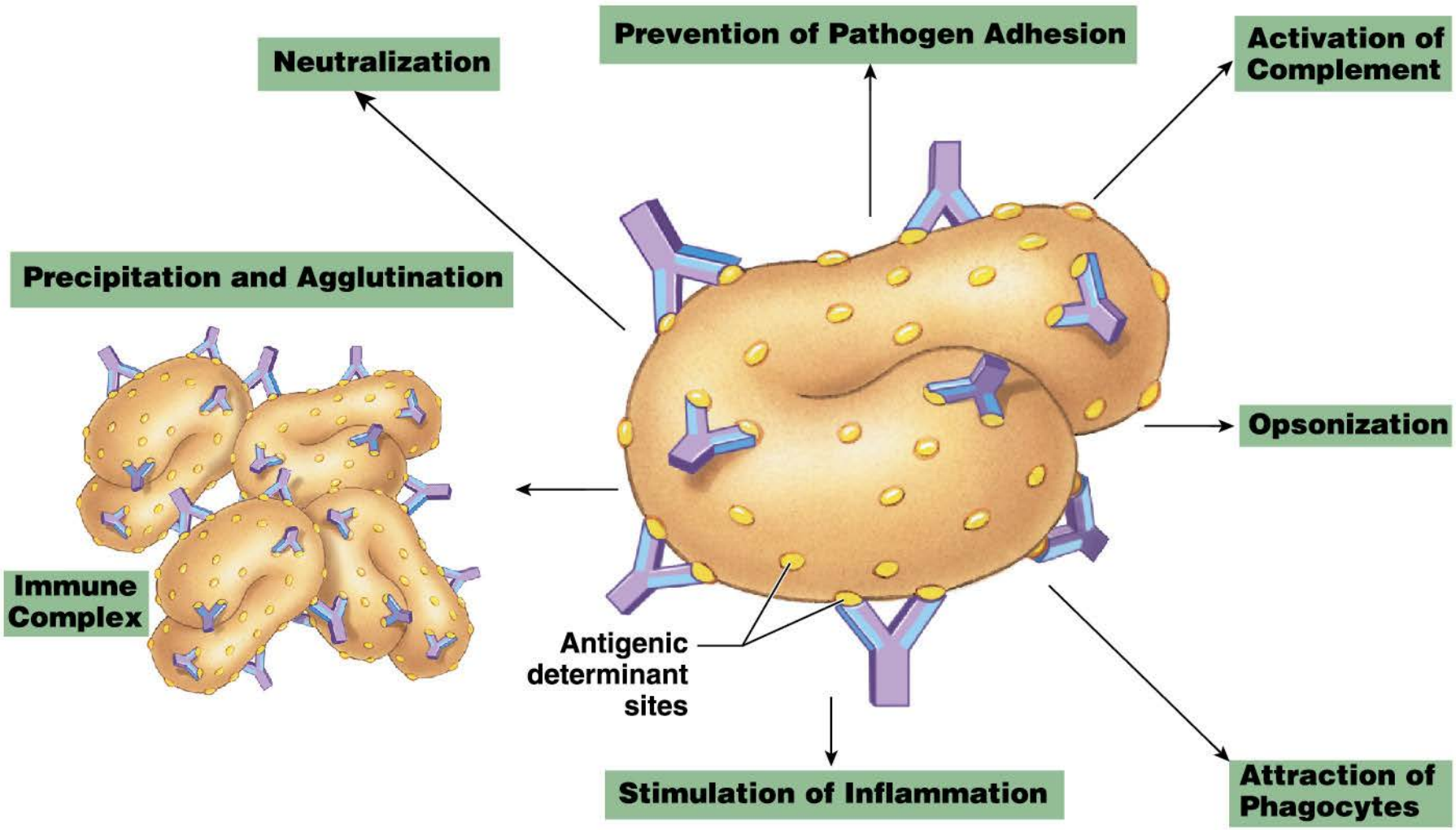
Antibody mechanisms



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Module 20.19: Review

A. List the ways that antigen-antibody complexes can destroy target antigens.
B. Define *opsonization*.
C. Which cells are involved in inflammation?

Learning Outcome: Explain the mechanisms by which antibodies destroy target antigens.

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Module 20.20: Clinical Module: Hypersensitivities are abnormal reactions to antigens

Hypersensitivities (allergies)

- Excessive immune responses to antigens
- Sudden increase in cellular activity and antibody titers
  - Neutrophils or cytotoxic T cells may destroy normal cells in addition to antigen
  - Antigen-antibody complex may trigger inflammation
  - Antigens triggering allergic reactions are called **allergens**

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Module 20.20: Allergies and anaphylaxis

Hypersensitivities (continued)

- Initial exposure to allergen
  - Causes sensitization and activation of B cells
  - Leads to production of large quantities of IgE
    - Tendency to produce IgE antibodies in response to specific allergens may be genetically determined
- Subsequent exposure to allergen
  - Causes massive stimulation of mast cells and basophils and a variety of localized or systemic reactions

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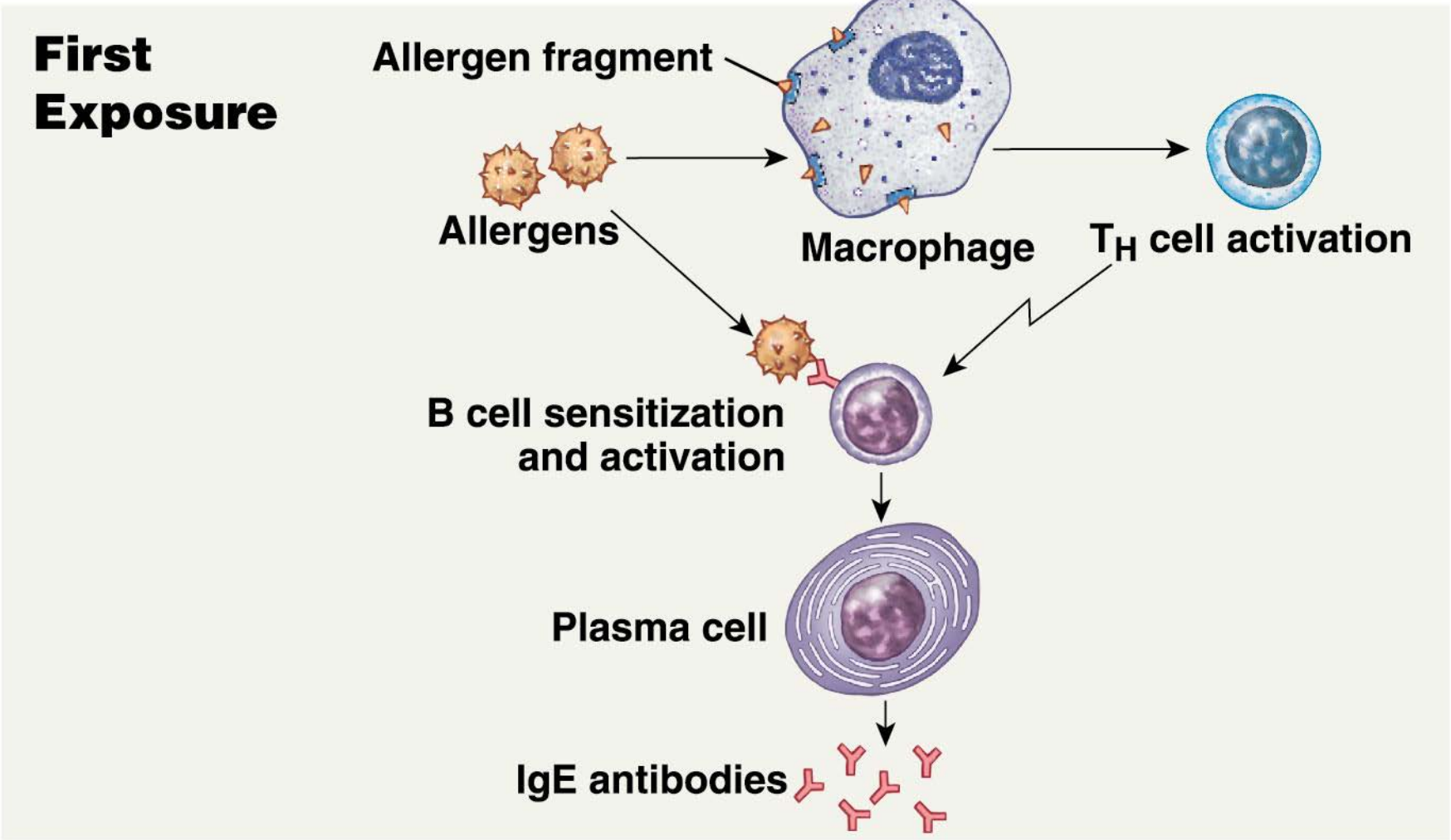
First exposure



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Module 20.20: Allergies and anaphylaxis

Hypersensitivities (continued)

- **Immediate hypersensitivity**
  - Rapid, severe response to an antigen
  - *Example:* **allergic rhinitis** (includes hay fever)
    - Inflammation of the nasal membranes
    - May affect 15 percent of U.S. population
    - Response restricted to body surface
  - Body's response to immediate hypersensitivity is called a **hypersensitivity reaction**

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Module 20.20: Allergies and anaphylaxis

Hypersensitivities (continued)

- Allergic reactions can be:
  - Localized (allergen at the body surface)
    - Causes localized inflammation, pain, and itching
    - *Example:* **allergic rhinitis**
  - Systemic (allergen in bloodstream)
    - Causes itching, swelling, and difficulty breathing (from airway constriction)
    - *Example:* **anaphylaxis** (*ana-*, again + *phylaxis*, protection)

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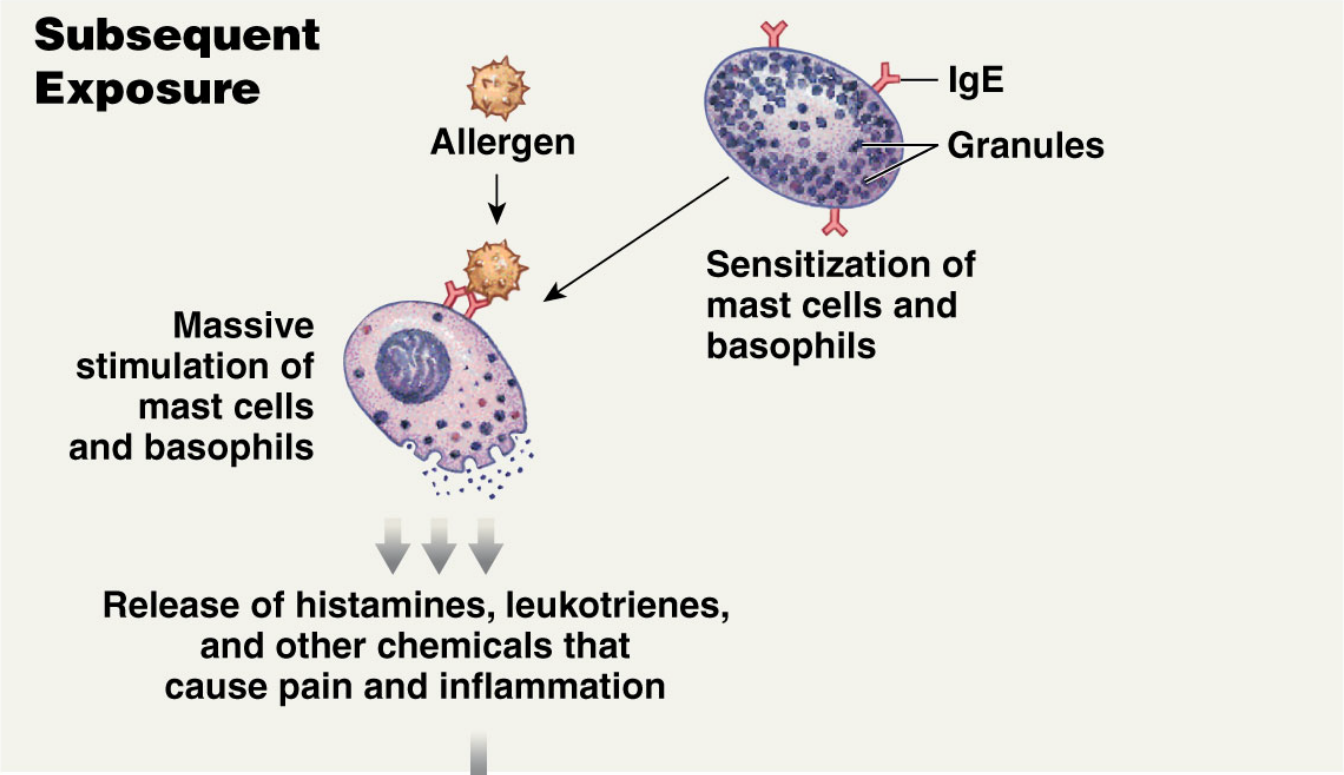
Subsequent exposure



Localized Allergic Reactions	Systemic Allergic Reactions
If the allergen is at the body surface: localized inflammation, pain, and itching Example: urticaria (hives)	If the allergen is in the bloodstream: itching, swelling, and difficulty breathing (due to airway constriction) Example: anaphylaxis

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Module 20.20: Allergies and anaphylaxis

Anaphylaxis

- A systemic hypersensitivity reaction
- Circulating allergen affects mast cells throughout the body
- Severe cases cause peripheral vasodilation
  - Causes drop in blood pressure that can lead to circulatory collapse
  - Response called **anaphylactic shock**

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Module 20.20: Review

A. Describe hypersensitivities.
B. Which chemicals do mast cells and basophils release when stimulated in an allergic reaction?
C. What is anaphylaxis?

Learning Outcome: Explain hypersensitivities, anaphylaxis, and the role of antibodies in each.

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Module 20.21: Innate immunity and adaptive immunity work together to defeat pathogens

Overview

- Exposure to antigens triggers both specific and nonspecific defenses
  - Neither branch works alone
  - Many times, activities from each branch will enhance the other
- Responses will vary based on antigen type

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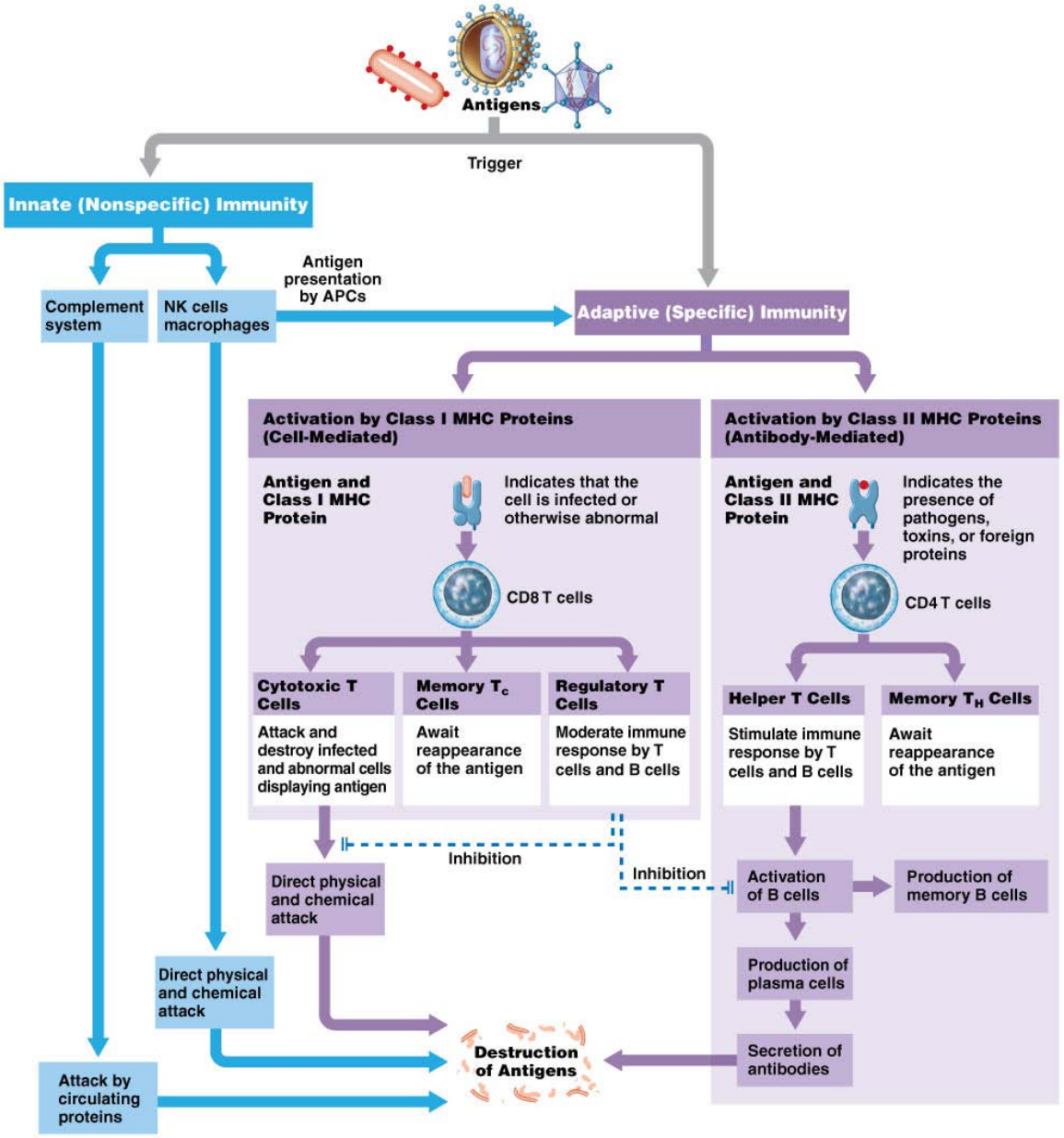
Innate and adaptive immunity



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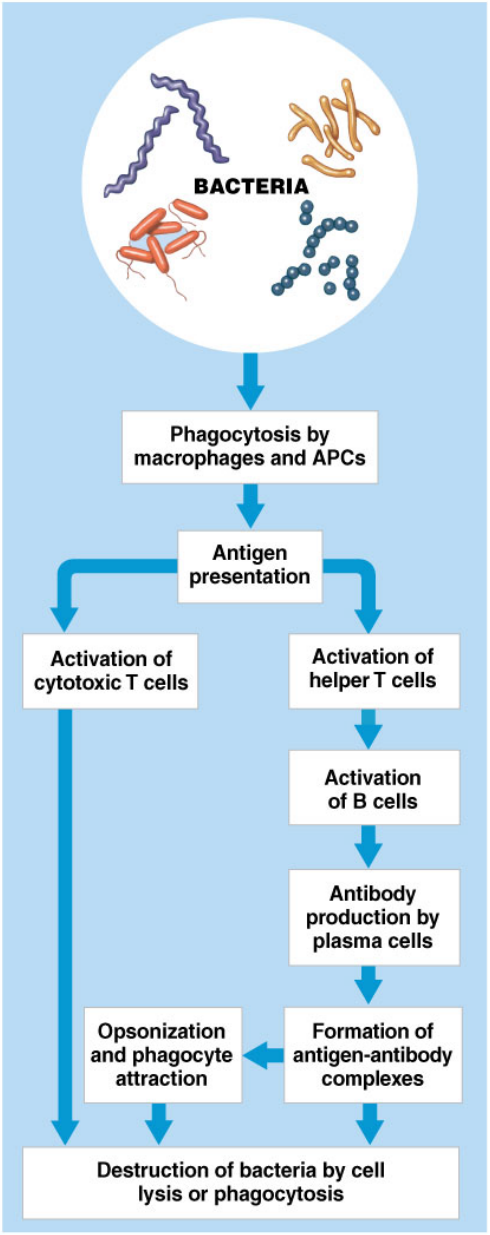
Module 20.21: Integrated immune response

Responses to bacterial and viral infection

- Overcoming a bacterial infection
  - Most effective defenses involve phagocytosis and antigen presentation by APCs



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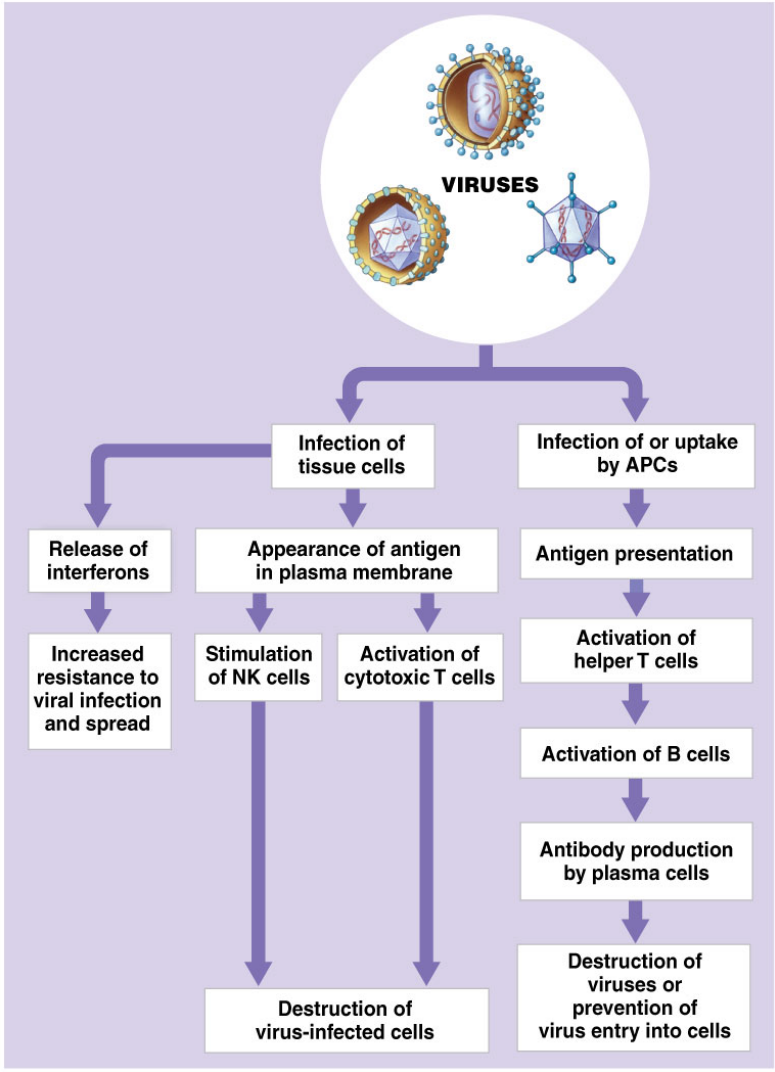
Module 20.21: Integrated immune response

Responses to bacterial and viral infection (continued)

- Overcoming a viral infection
  - Cytotoxic T cells and NK cells can be activated by direct contact with virus-infected cells
  - Process also involves antigen presentation and subsequent responses



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Module 20.21: Review

A. Which T cells contain CD8 markers? CD4 markers?
B. Which cells produce antibodies?
C. Which cells can be activated by direct contact with virus-infected cells?

Learning Outcome: Summarize the integration of innate and adaptive immunity.

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Module 20.22: Clinical Module: Immune disorders involving either overactivity . . .

Excessive or misdirected immune response

- **Autoimmune disorders**
  - Malfunction of the body's self recognition system
  - Activated B cells make antibodies against "self" antigens or body cells and tissues
    - Called **autoantibodies**
  - May result from similarity of foreign antigen to body cells
    - *Example*: Protein in measles virus contains amino acid sequences similar to those of myelin proteins, so antibodies targeting the viruses may also target myelin sheaths (likely mechanism for multiple sclerosis)

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Module 20.22: Immune disorders

Excessive or misdirected immune response (continued)

- **Autoimmune disorders** (continued)
  - Risk increases if a person has an unusual type of MHC protein
  - Examples of autoimmune disorders
    - **Thyroiditis** (inflammation resulting from autoantibodies attacking thyroglobulin)
    - **Rheumatoid arthritis** (autoantibodies attack connective tissues around joints)
    - **Type 1 diabetes mellitus** (autoantibodies attack pancreatic islet cells)
    - Multiple sclerosis (autoantibodies attack myelin)

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Module 20.22: Immune disorders

Excessive or misdirected immune response (continued)

- **Transplant rejection**
  - Recipient cytotoxic T cells become activated and attack MHC proteins of donated material
  - Reduction in immune response sensitivity (**immunosuppression**) by drugs can increase transplant success
    - *Example*: **Cyclosporin** inhibits helper T cells
- **Hypersensitivities**

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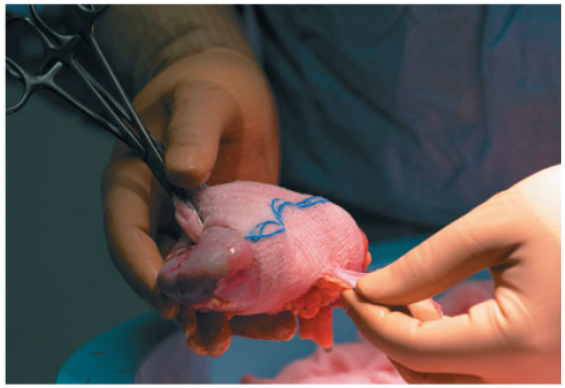
Excessive or misdirected immune response



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Module 20.22: Clinical Module: . . . or underactivity can be harmful

Inadequate immune response

- **Immunodeficiency diseases**
  - Result from:
    1. Problems with lymphoid organ and tissue development
    2. An infection with a virus that depresses immune function
       - Most common immunodeficiency disease is **acquired immunodeficiency syndrome** (**AIDS**)
    3. Treatment with, or exposure to, immunosuppressive agents such as radiation or drugs

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Module 20.22: Immune disorders

Inadequate immune response (continued)

- **Immunodeficiency diseases** (continued)
  - **Acquired immunodeficiency syndrome** (**AIDS**)
    - Caused by **human immunodeficiency virus** (**HIV**)
    - Virus binds to CD4 proteins and infects helper T cells
      - Infected cells synthesize and release new viral proteins
      - Helper T cells are destroyed by virus or immune defenses
        - Impairs both cell-mediated and antibody-mediated responses
      - Suppressor T cells not affected

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Module 20.22: Immune disorders

Inadequate immune response (continued)

- **Immunodeficiency diseases** (continued)
  - **Acquired immunodeficiency syndrome** (**AIDS**) (continued)
    - Body more vulnerable to microbial invaders, **opportunistic infections**, and cancer
    - Spread by contact with body fluids
    - Infects 33 million people worldwide, with 2 million deaths each year

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Module 20.22: Immune disorders

Inadequate immune response (continued)

- **Age-related reductions in immune activity**
  - Immune system is less effective with age
  - Thymus shrinks, and thymic hormone levels decrease
  - Increased susceptibility to viral and bacterial infections
    - T cells become less responsive
      - Fewer cytotoxic T cells respond
    - Number of T helper cells reduced
    - B cells less responsive
      - Antibody levels slower to rise after antigen exposure
    - Vaccinations highly recommended

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Module 20.22: Immune disorders

Inadequate immune response (continued)

- **Age-related reductions in immune activity** (continued)
  - Increased incidence of cancer
    - NK cells reduced and immune surveillance compromised

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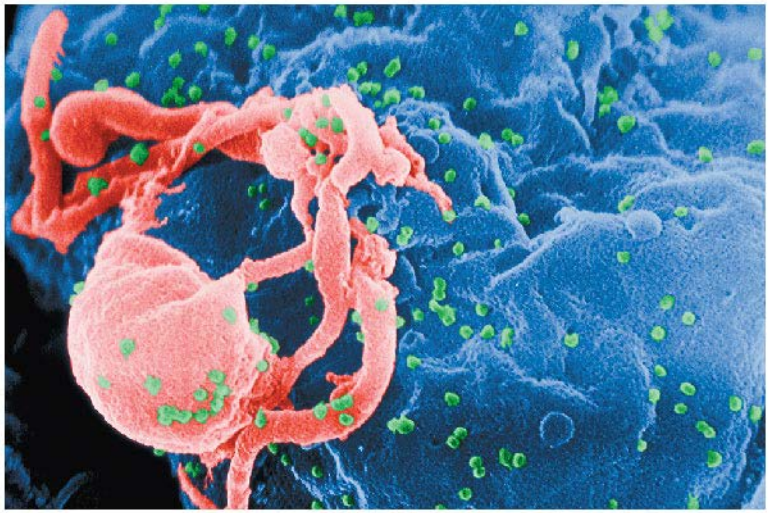
Inadequate immune response



HIV (green) budding from an infected T_H cell

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Module 20.22: Review

1. Define *autoimmune disorders*.
2. Describe immunodeficiency diseases.
3. Provide a plausible explanation for the increased incidence of cancer in the elderly.

Learning Outcome: Explain autoimmune disorders, transplanted rejection, and immunodeficiency diseases, and describe age-related changes in the immune response.

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