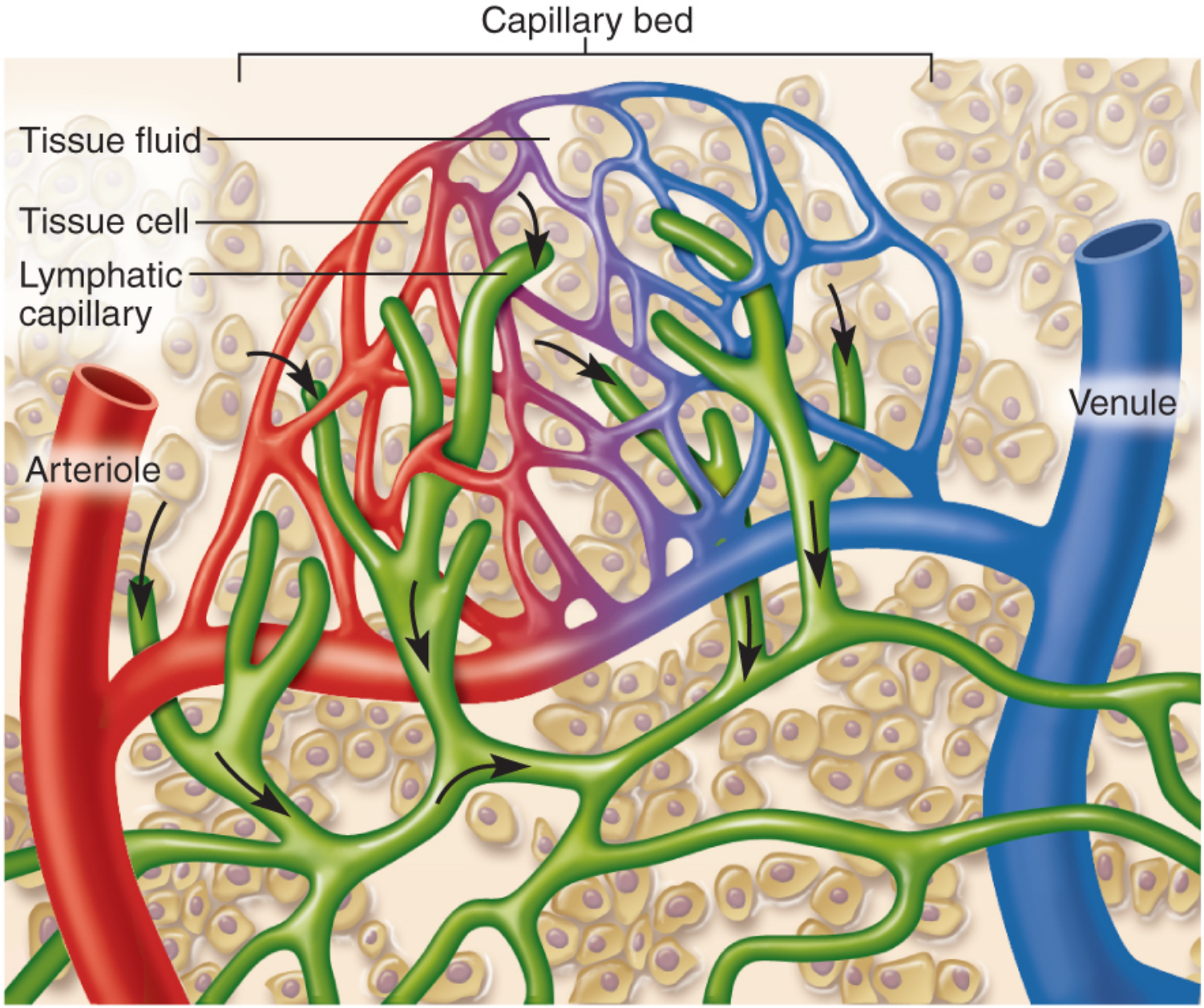
Lymphatic and Immune Systems

- **immune system** – not an organ system, but a population of cells that inhabit all of our organs and defend the body from agents of disease
  - especially concentrated in the true organ system – **lymphatic system**
    - network of organs and vein-like vessels that recover fluid
    - inspect it for disease agents
    - activate immune responses
    - return the fluid to the bloodstream



(a)

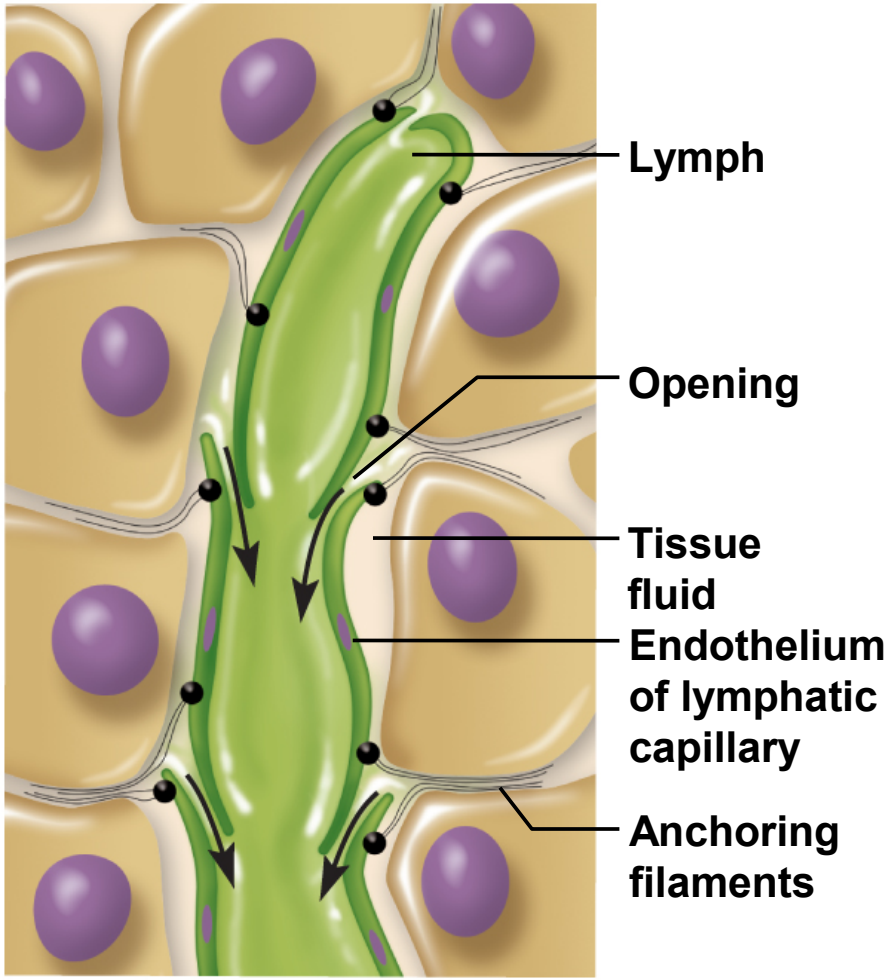
Components of the Lymphatic System

- **lymph**
  - the recovered fluid
- **lymphatic vessels**
  - transport the lymph
- **lymphatic tissues**
  - composed of aggregates of lymphocytes and macrophages that populate many organs in the body
- **lymphatic organs**
  - defense cells are especially concentrated in these organs
  - separated from surrounding organs by connective tissue capsules

Lymph and Lymphatic Capillaries

- **lymph**
  - clear, colorless fluid, similar to plasma, but much less protein
  - extracellular fluid drawn into lymphatic capillaries
- **lymphatic capillaries**
  - penetrate nearly every tissue of the body
    - absent from central nervous system, cartilage, cornea, bone and bone marrow
  - gaps allow bacteria and cells entrance to lymphatic capillary
  - endothelium creates valve-like flaps that open when interstitial fluid pressure is high, and close when it is low

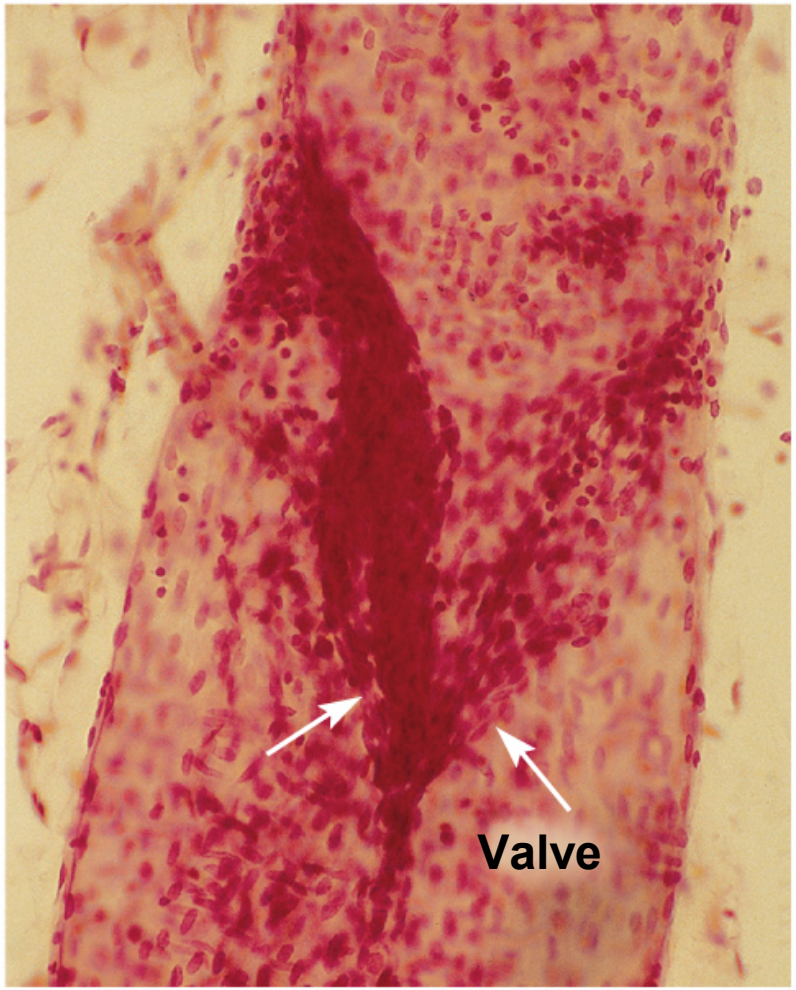
Lymphatic Capillary



(b)

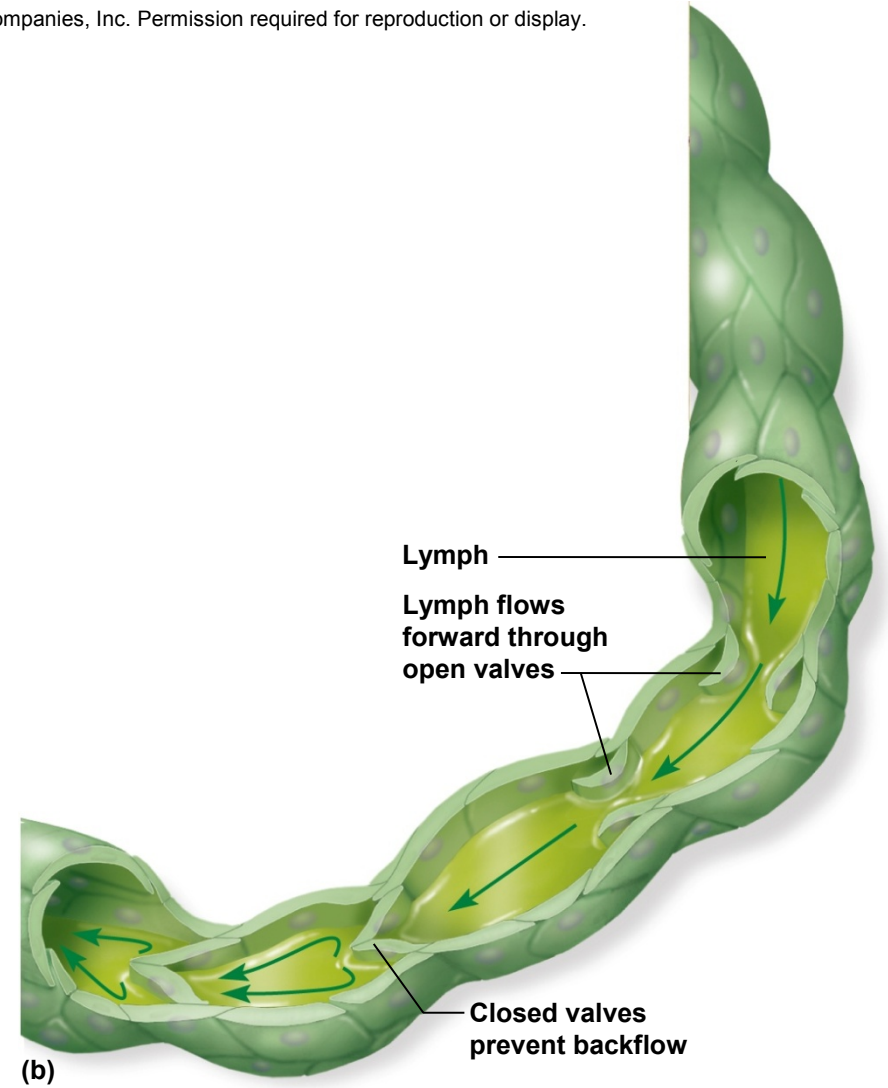
Figure 21.3b

Valve in a Lymphatic Vessel



(a)

Figure 21.4a

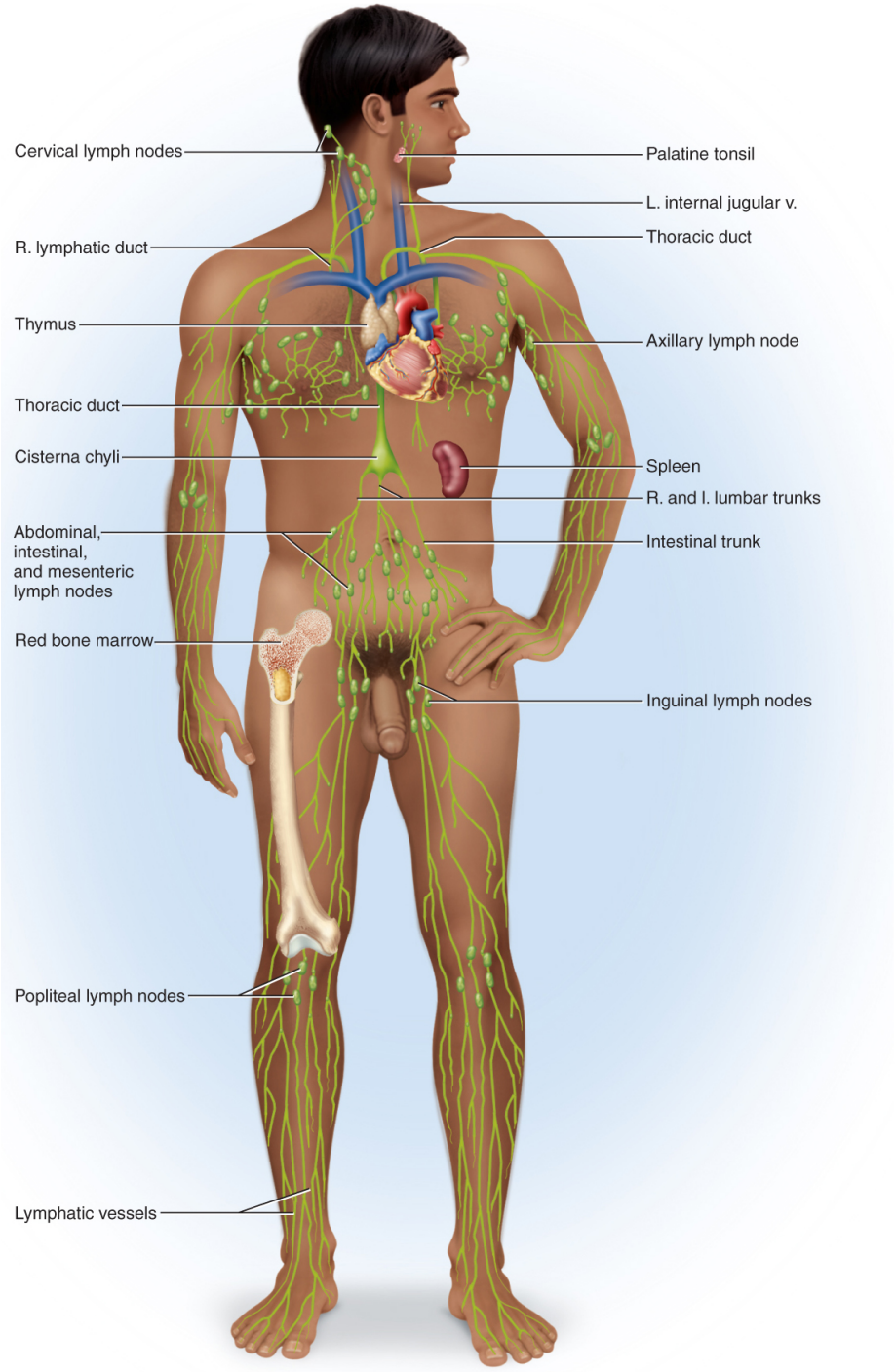


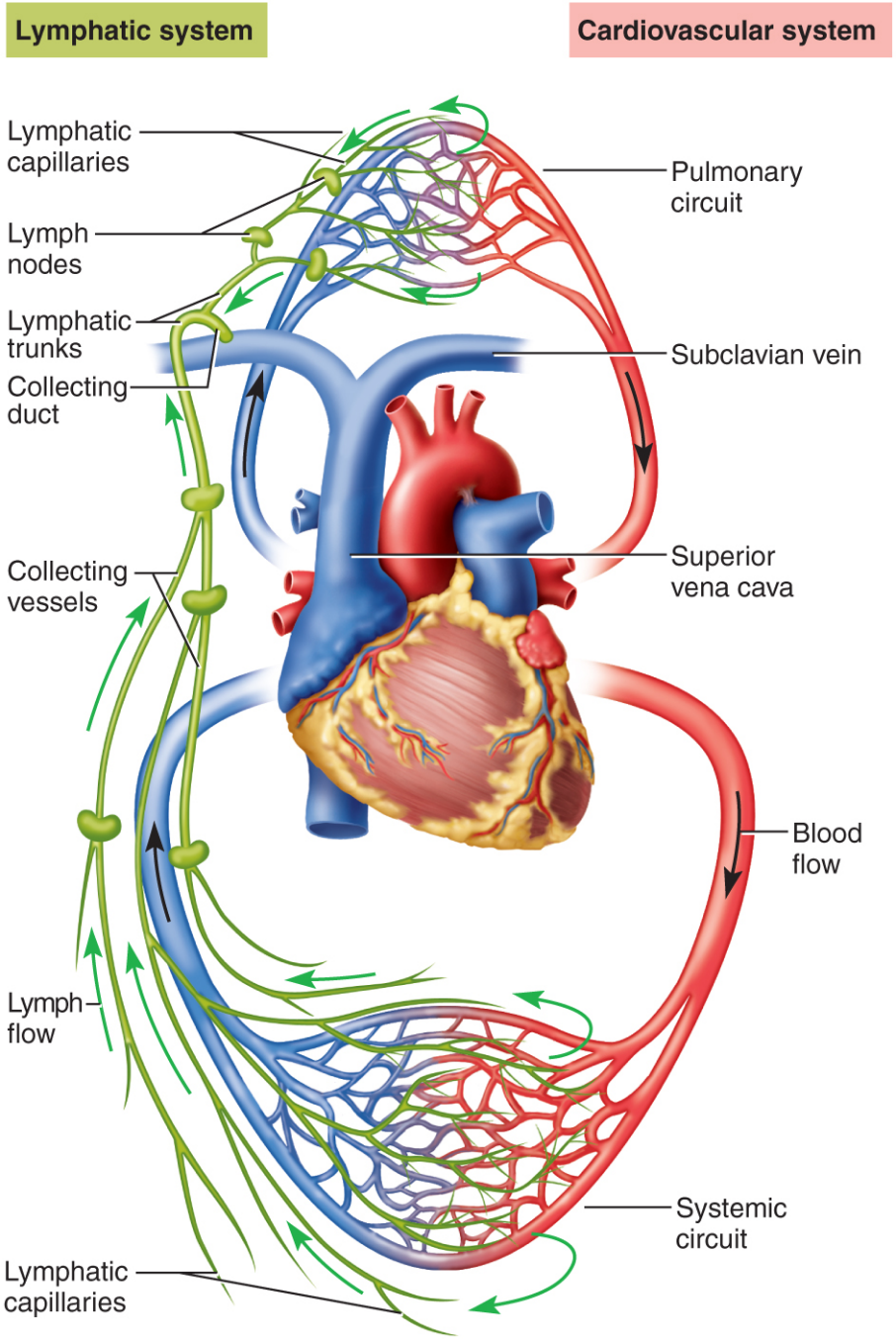
(b)

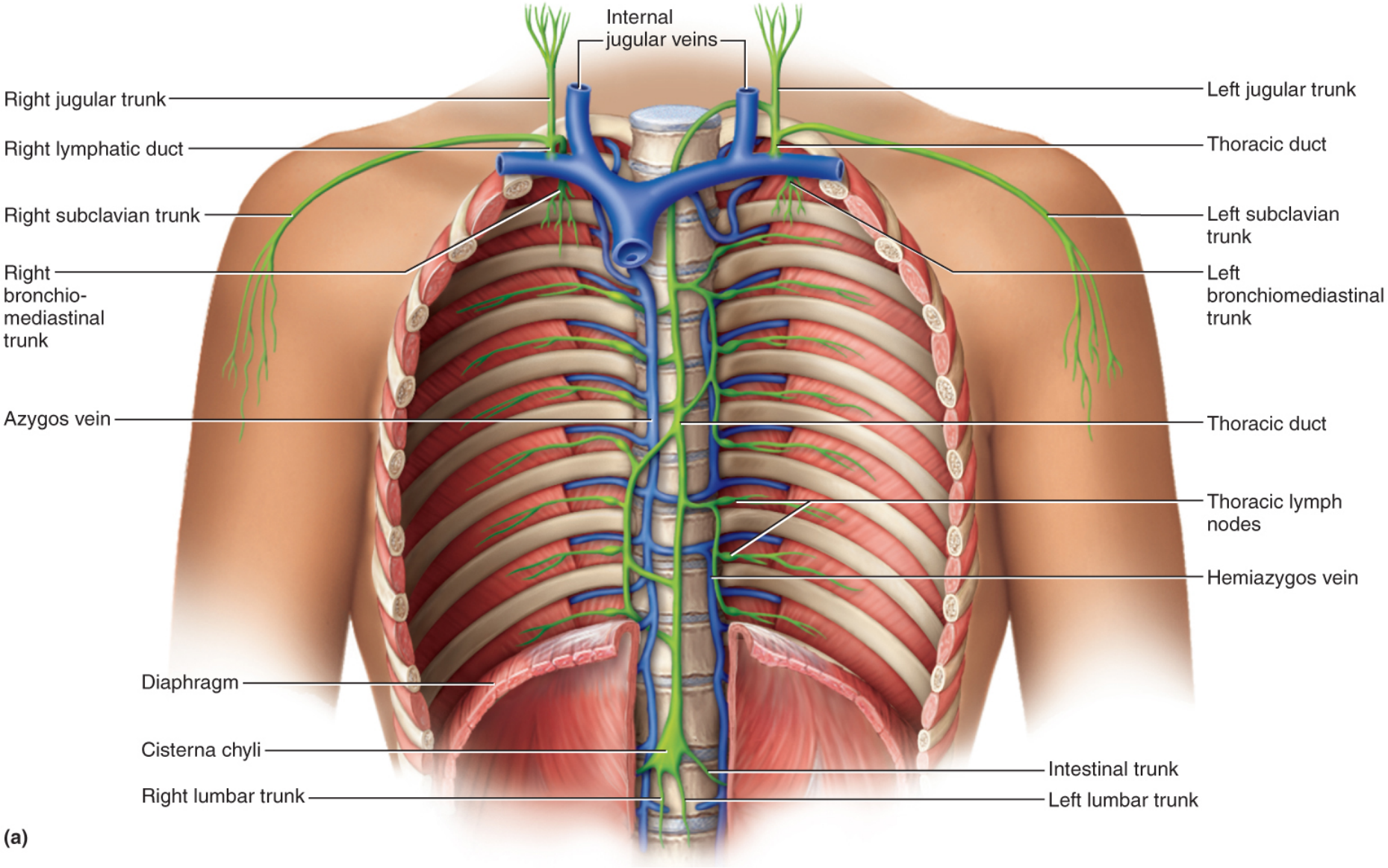
Figure 21.4b

Route of Lymph Flow

- **lymphatic capillaries**
- **collecting vessels**: course through many lymph nodes
- **six lymphatic trunks**: drain major portions of body
- **two collecting ducts**:
  - **right lymphatic duct** – receives lymph from right arm, right side of head and thorax; empties into right subclavian vein
  - **thoracic duct** - larger and longer, receives lymph from below diaphragm, left arm, left side of head, neck, and thorax; empties into left subclavian vein
- **subclavian veins**







(a)

Lymphatic Tissue

- **lymphatic tissue** – aggregations of lymphocytes in the connective tissues of mucous membranes and various organs
- **diffuse lymphatic tissue** – simplest form
  - respiratory, digestive, urinary, and reproductive tracts
  - **mucosa-associated lymphatic tissue (MALT)**
- **lymphatic nodules**
  - lymph nodes, tonsils, and appendix
  - **Peyer patches** – dense clusters in the ileum, the distal portion of the small intestine

Lymphatic Nodule

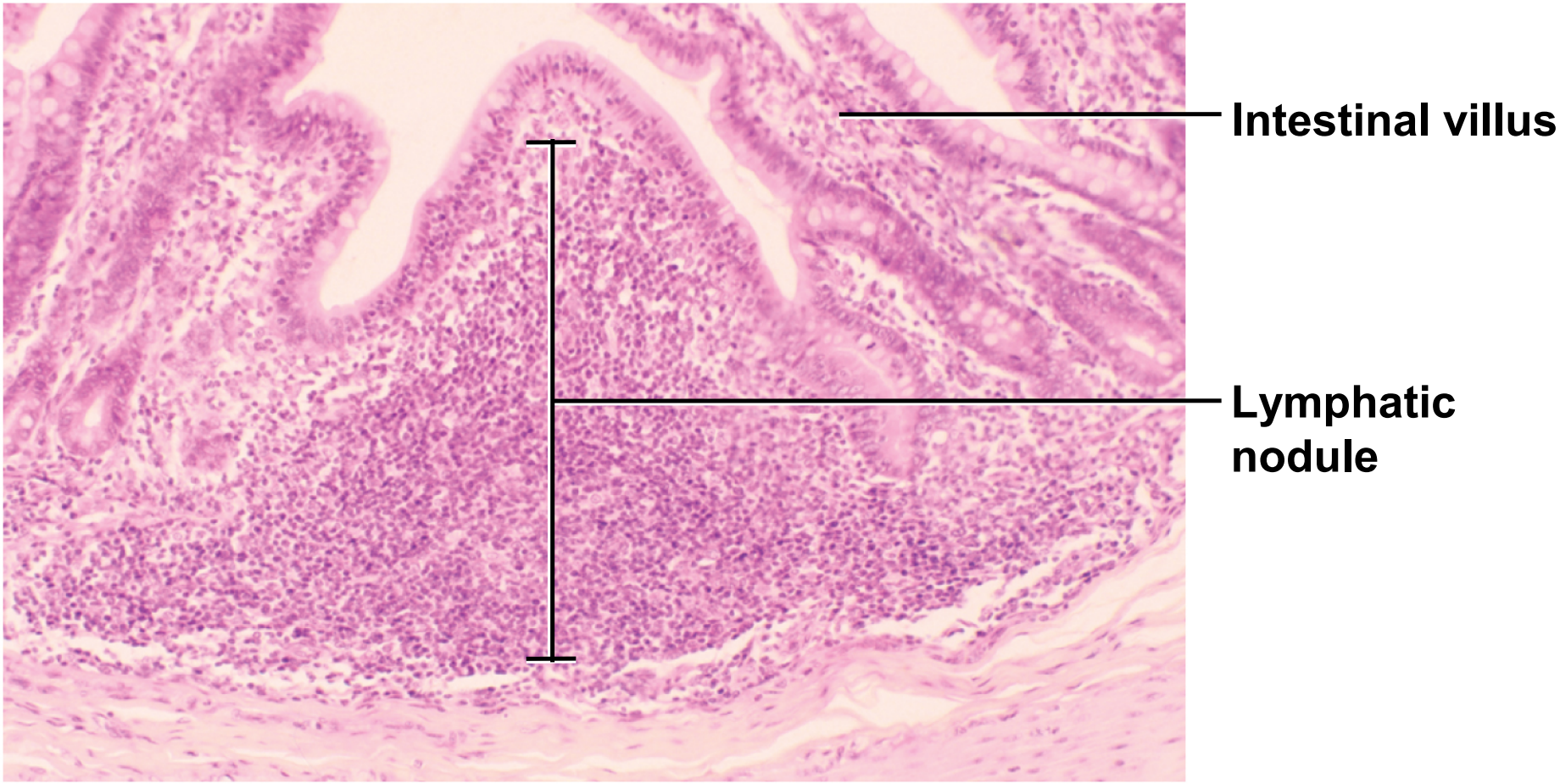


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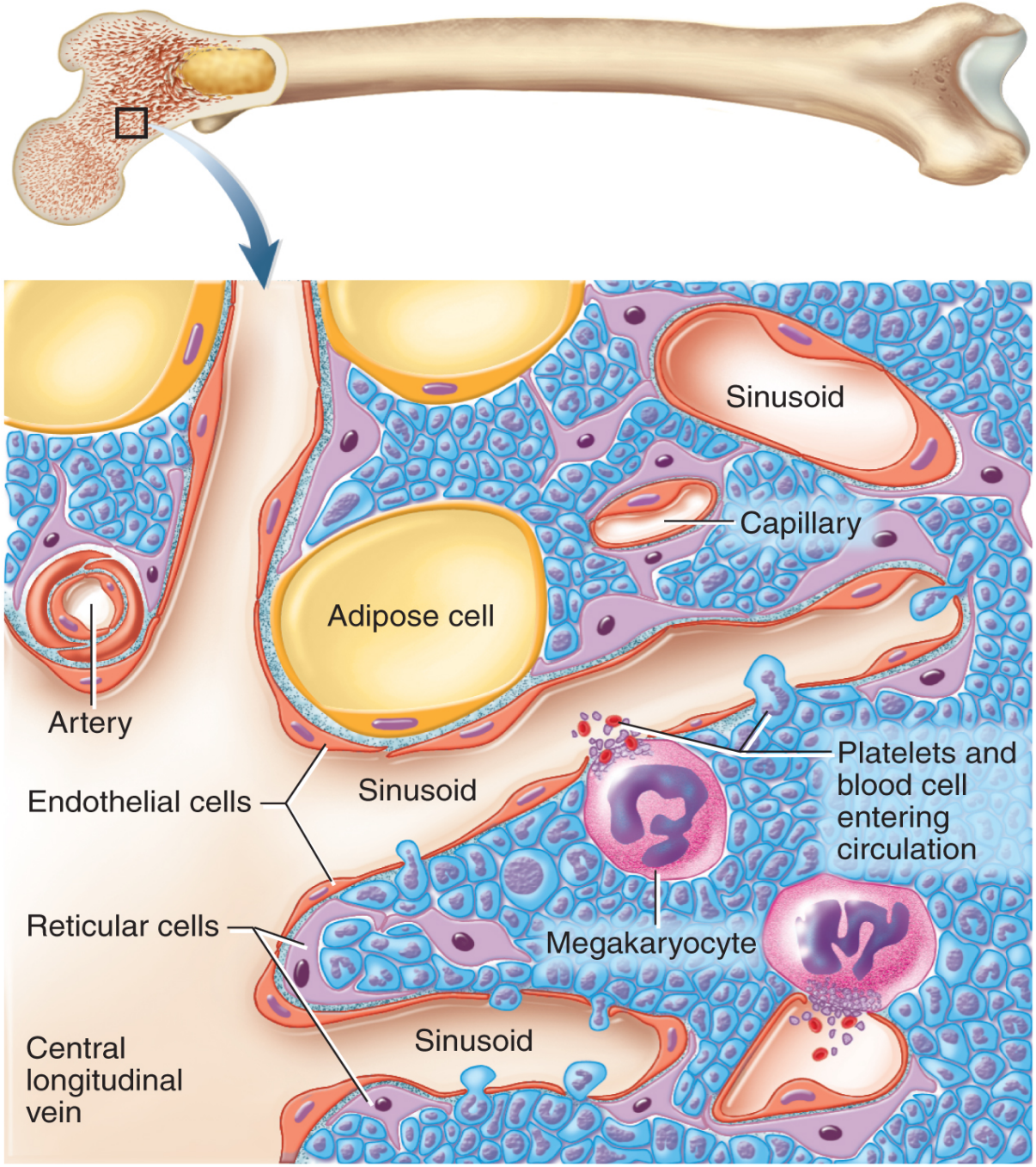
Figure 21.8

Lymphatic Organs

- **connective tissue capsule** that separates the lymphatic tissue from neighboring tissues
- **primary lymphatic organs**
  - **red bone marrow** and **thymus**
  - site where T and B cells become **immunocompetent** – able to recognize and respond to antigens
- **secondary lymphatic organs**
  - **lymph nodes**, **tonsils**, and **spleen**
  - immunocompetent cells populate these tissues

Red Bone Marrow

- red bone marrow is involved in **hemopoiesis** (blood formation) and **immunity**
  - as blood cells mature, they push their way through the reticular and endothelial cells to enter the sinus and flow away in the blood stream



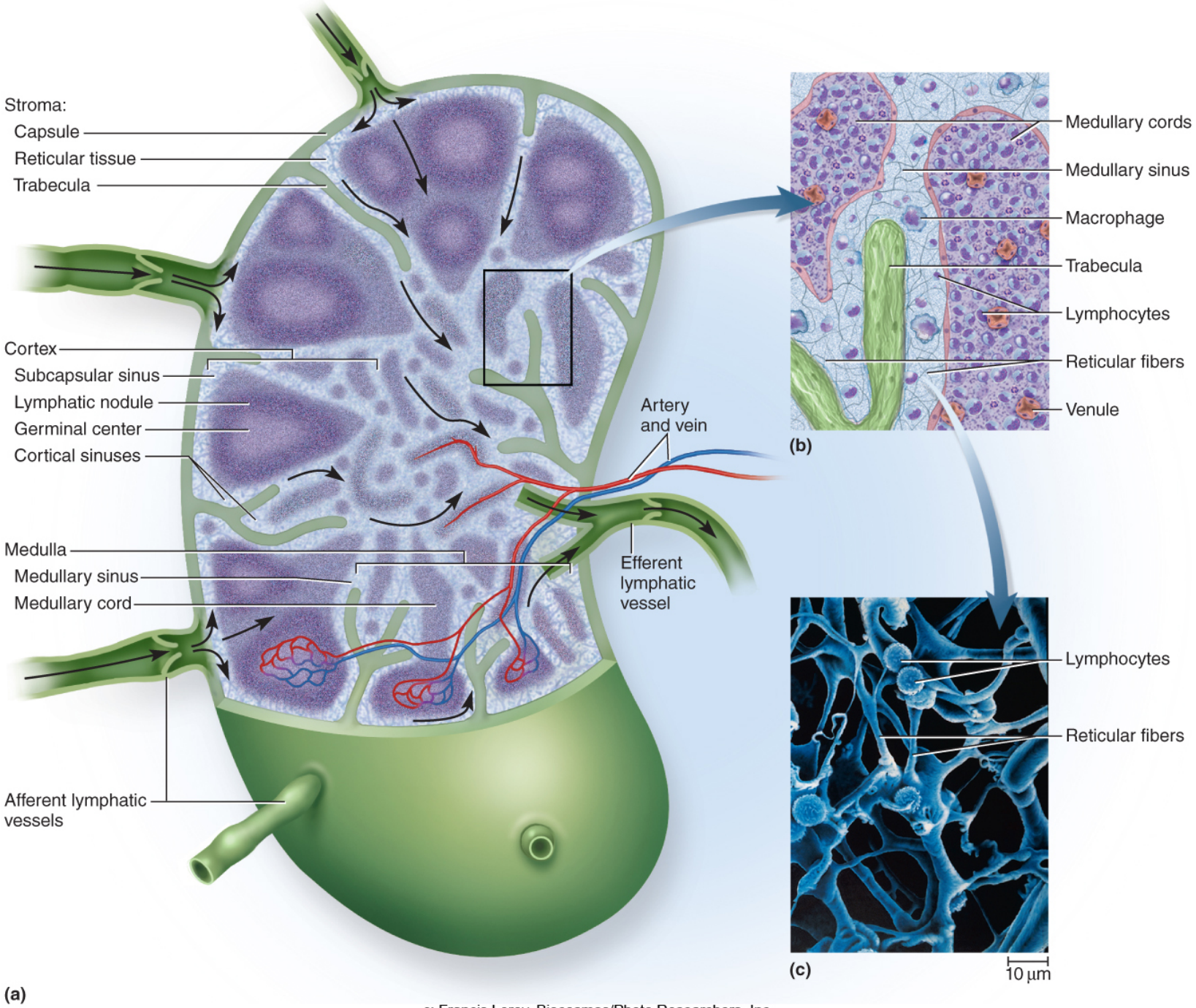
Thymus

- **thymus** – member of the endocrine, lymphatic, and immune systems
  - houses developing lymphocytes
  - secretes hormones regulating their activity
  - lobes have cortex and medulla populated by T lymphocytes

Lymph Node

- **lymph nodes**
  - cleanse the lymph
  - act as a site of T and B cell activation

- **parenchyma** divided into **cortex** and **medulla**
  - **germinal centers** where B cells multiply and differentiate into plasma cells
- several **afferent lymphatic vessels** lead into the node along its convex surface
  - lymph leaves the node through one to three **efferent lymphatic vessels**



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Lymph Nodes and Metastatic Cancer

- **Metastasis -** primary tumor cell travel to other sites in the body, and establish new tumors.
  - metastasizing cancer cells can easily enter the lymphatic vessels
  - tend to lodge in the first lymph node they encounter
  - multiply there and eventually destroy the node
    - swollen, firm, and usually painless
  - tend to spread to the next node downstream
  - treatment of breast cancer is lumpectomy, mastectomy along with removal of nearby axillary nodes

Tonsils

- **tonsils** – patches of lymphatic tissue located at the entrance to the pharynx
  - guard against ingested or inhaled pathogens

The Tonsils

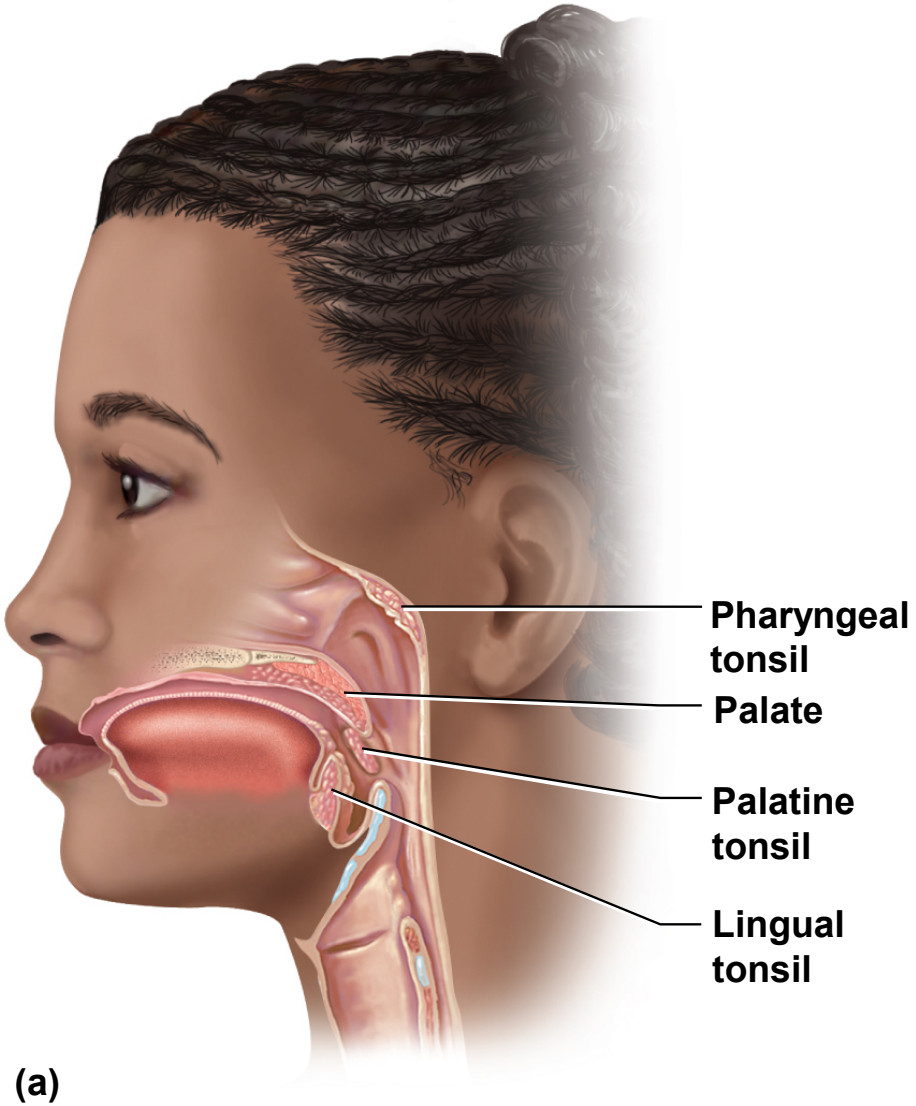


Figure 21.13 a

Spleen

- **spleen** – the body's largest lymphatic organ
- **parenchyma** exhibits two types of tissue:
  - **red pulp** - sinuses filled with erythrocytes
  - **white pulp** - lymphocytes, macrophages surrounding small branches of splenic artery
- functions
  - blood production in fetus
  - blood reservoir
  - 'erythrocyte graveyard' - RBC disposal
  - white pulp monitors blood for foreign antigens

Spleen

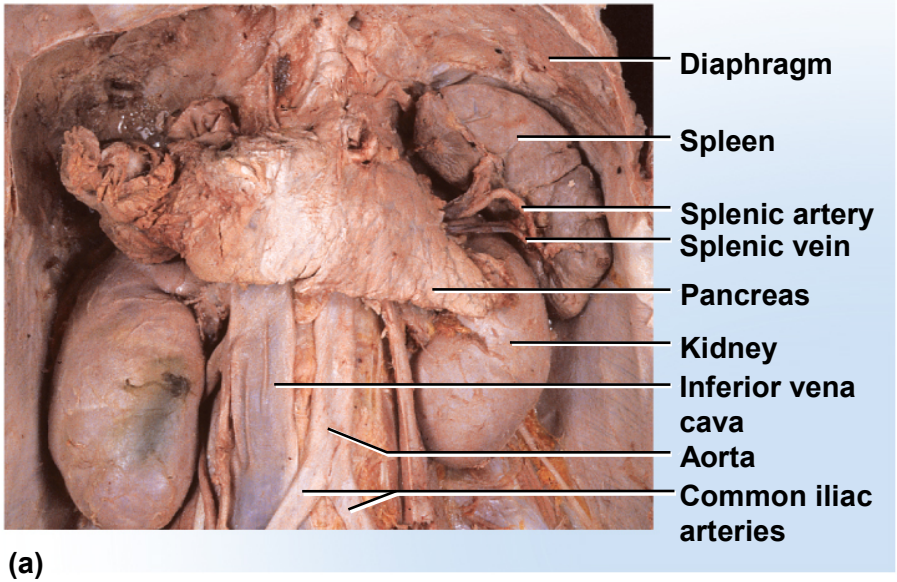


Figure 21.14a

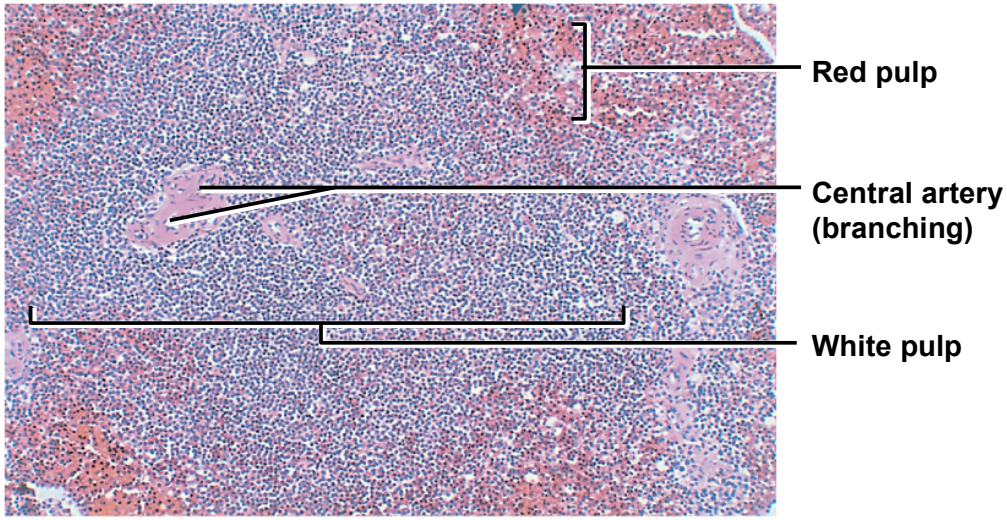


Figure 21.14c

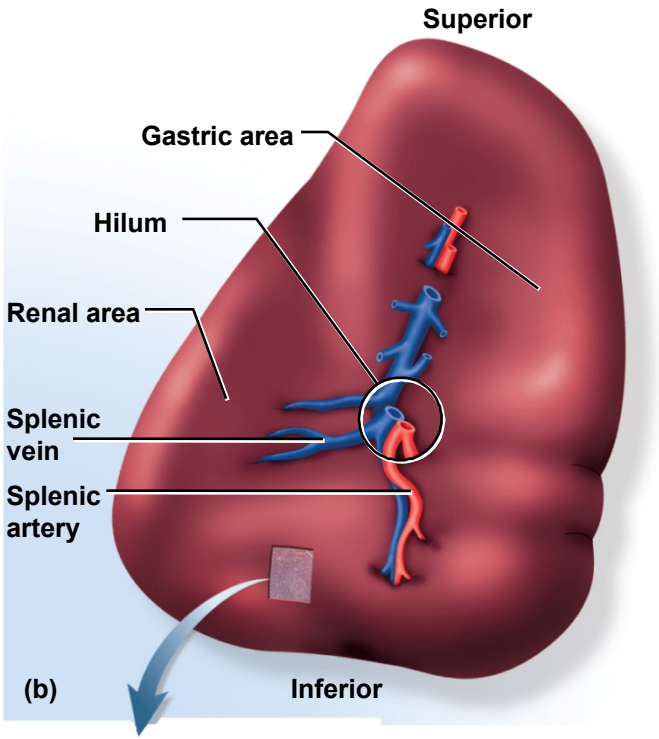


Figure 21.14b

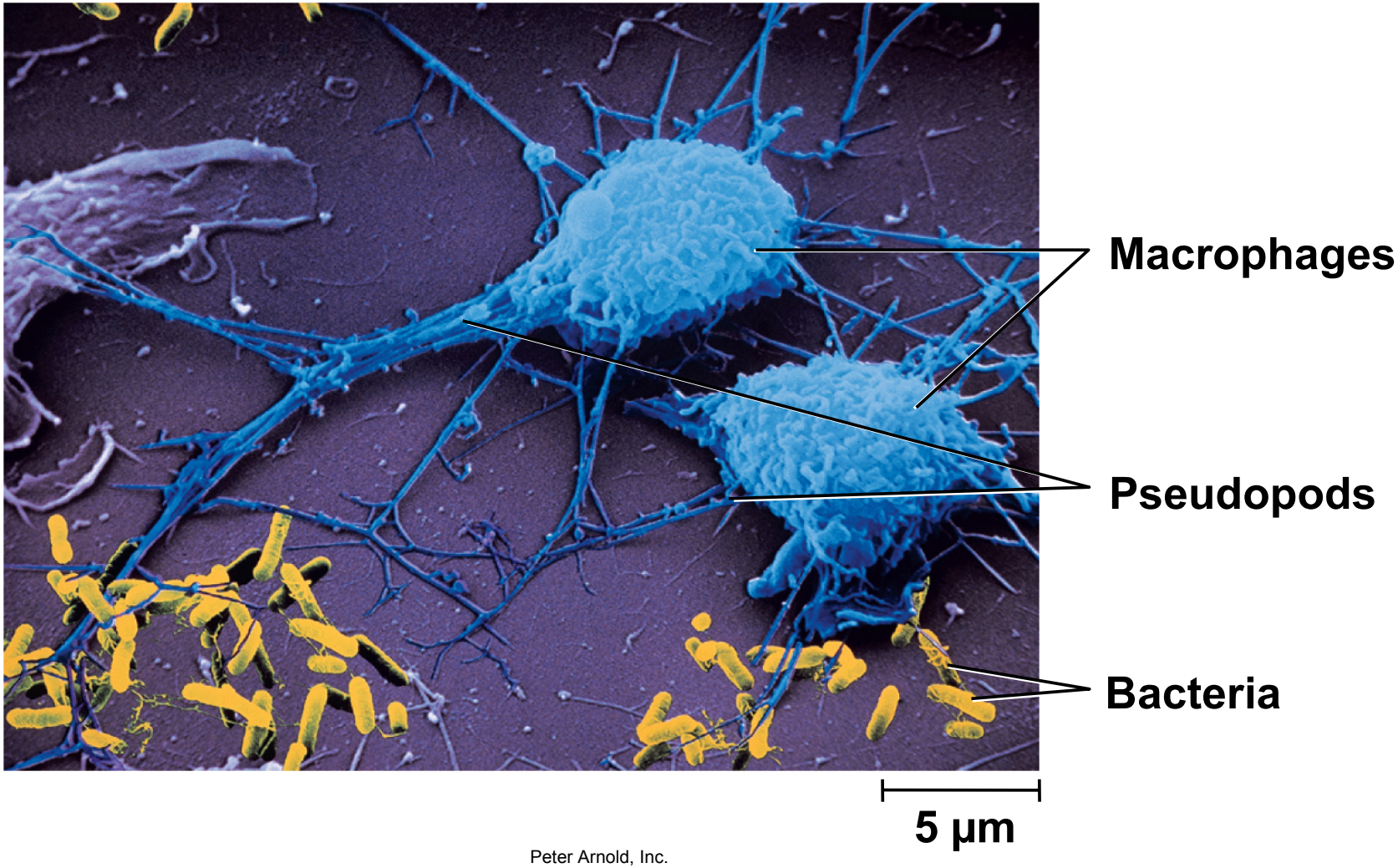
Lymphatic Cells

- **natural killer (NK) cells**
  - large lymphocytes that attack and destroy bacteria, transplanted tissue, host cells infected with viruses or have turned cancerous
  - responsible for immune surveillance
- **T lymphocytes (T cells)**
  - mature in thymus
- **B lymphocytes (B cells)**
  - activation causes proliferation and differentiation into **plasma cells** that produce **antibodies**

Lymphatic Cells

- **macrophages**
  - very large, avidly phagocytic cells of the connective tissue
  - develop from monocytes
  - phagocytize tissue debris, dead neutrophils, bacteria, and other foreign matter
  - process foreign matter and display antigenic fragments to certain T cells alerting the immune system to the presence of the enemy
  - antigen presenting cells (APCs)
- **dendritic cells**
  - branched, mobile APCs found in epidermis, mucous membranes, and lymphatic organs
  - alert immune system to pathogens that have breached their surface
- **reticular cells**
  - act as APCs in the thymus

Macrophages



Peter Arnold, Inc.

Figure 21.7

Defenses Against Pathogens

- **pathogens** – environmental agents capable of producing disease
  - infectious organisms, toxic chemicals, and radiation
- **three lines of defenses** against pathogens:
  - **first line of defense** – external barriers, skin and mucous membranes
  - **second line of defense** – several nonspecific defense mechanisms
    - leukocytes and macrophages, antimicrobial proteins, immune surveillance, inflammation, and fever
    - effective against a broad range of pathogens
  - **third line of defense** – the immune system
    - defeats a pathogen, and leaves the body of a 'memory' of it so it can defeat it faster in the future

Neutrophils

- wander in connective tissue killing bacteria
  - phagocytosis and digestion
  - produces a cloud of bactericidal chemicals
- create a **killing zone**
  - degranulation
    - lysosomes discharge into tissue fluid
  - **respiratory burst** – neutrophils rapidly absorb oxygen
    - **toxic chemicals** are created ($O_2^{\cdot -}$, H_2O_2)
  - kill more bacteria with toxic chemicals than phagocytosis

Eosinophils

- found especially in the mucous membranes
- stand guard against **parasites**, **allergens** (allergy causing agents), and other pathogens
- kill tapeworms and roundworms by producing superoxide, hydrogen peroxide, and toxic proteins
- phagocytize **antigen-antibody complexes**

Basophils

- secrete chemicals that aid mobility and action of WBC other leukocytes
  - **leukotrienes** – activate and attract neutrophils and eosinophils
  - **histamine** – a vasodilator which increases blood flow
    - speeds delivery of leukocytes to the area
  - **heparin** – inhibits the formation of clots
    - would impede leukocyte mobility

Lymphocytes

- three basic categories
- circulating blood contains
  - 80% **T cells**
  - 15% **B cells**
  - 5% **NK cells**
- many diverse functions

Monocytes

- **monocytes** - emigrate from the blood into the connective tissue and transform into **macrophages**
- **macrophage system** – all the body's avidly phagocytic cells, except leukocytes
  - **wandering macrophages** – actively seeking pathogens
    - widely distributed in loose connective tissue
  - **fixed macrophages** – phagocytize only pathogens that come to them
    - **microglia** – in central nervous system
    - **alveolar macrophages** – in lungs
    - **hepatic macrophages** – in liver

Antimicrobial Proteins

- proteins that inhibit microbial reproduction and provide short-term, nonspecific resistance to pathogenic bacteria and viruses

- two families of antimicrobial proteins:
  - **interferons**
  - **complement system**

Interferons

- **interferons** - secreted by certain cells infected by viruses
  - of no benefit to the cell that secretes them
  - alert neighboring cells and protect them from becoming infected
  - also activates NK cells and macrophages
    - destroy infected cell before they can liberate a swarm of newly replicated viruses
  - activated NK cells destroy malignant cells

Complement System

- **complement system** – a group of 30 or more globular proteins
  - synthesized mainly by the liver
  - circulate in the blood in inactive form
  - activated by presence of the pathogen
  - activated complement brings about four methods of pathogen destruction
    - **inflammation**
    - **immune clearance**
    - **phagocytosis**
    - **cytolysis**

Complement System

- **classical pathway**
  - requires antibody molecule to get started
  - thus part of specific immunity
- **alternative pathway**
  - nonspecific, do not require antibody

- **lectin pathway**
  - **lectins –** plasma proteins that bind to carbohydrates
    - bind to certain sugars of a microbial cell surface

Complement System

- mechanisms of action of complement proteins
  - **inflammation**
    - stimulates mast cells and basophils to secrete histamine and other inflammatory chemicals
    - activates and attracts neutrophils and macrophages
  - **immune clearance**
    - C3b binds with antigen-antibody complexes to red blood cells
    - these RBCs circulate through the liver and spleen
    - macrophages of those organs strip off and destroy the Ag-Ab complexes leaving RBCs unharmed
    - principal means of clearing foreign antigens from the bloodstream

Complement System

- mechanisms of action of complement proteins
  - **phagocytosis**
    - neutrophils and macrophages **cannot phagocytize "naked"** bacteria, viruses, or other pathogens
    - C3b assist them by **opsonization**
      - coats microbial cells and serves as binding sites for phagocyte attachment
  - **cytolysis**
    - C3b splits other complement proteins
    - bind to enemy cell
    - attract more complement proteins – **membrane attack complex** forms
      - forms a hole in the target cell
      - electrolytes leak out, water flows in rapidly, and **cell ruptures**

Membrane Attack Complex

- complement proteins form ring in plasma membrane of target cell causing cytolysis

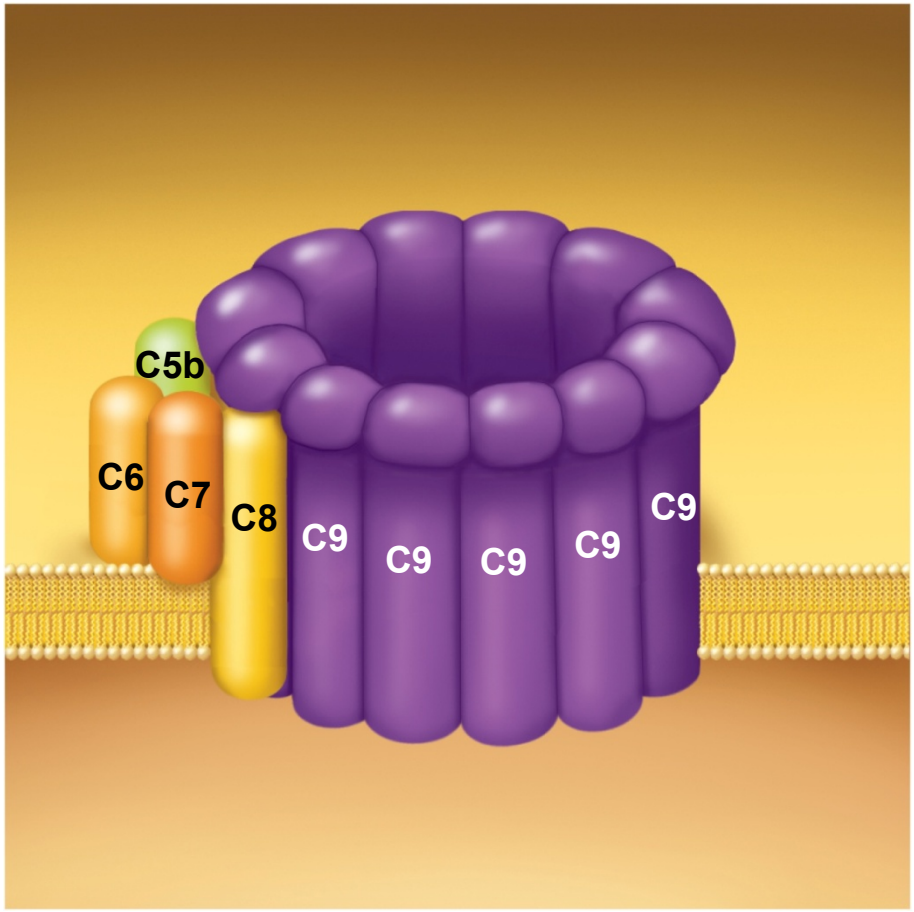


Figure 21.16

Immune Surveillance

- **natural (NK) killer cells** continually patrol the body on the lookout for pathogens and diseased host cells.
- **natural killer (NK) cells** attack and destroy:
  - bacteria, cells of transplanted organs, cells infected with viruses, and cancer cells

Action of NK cell

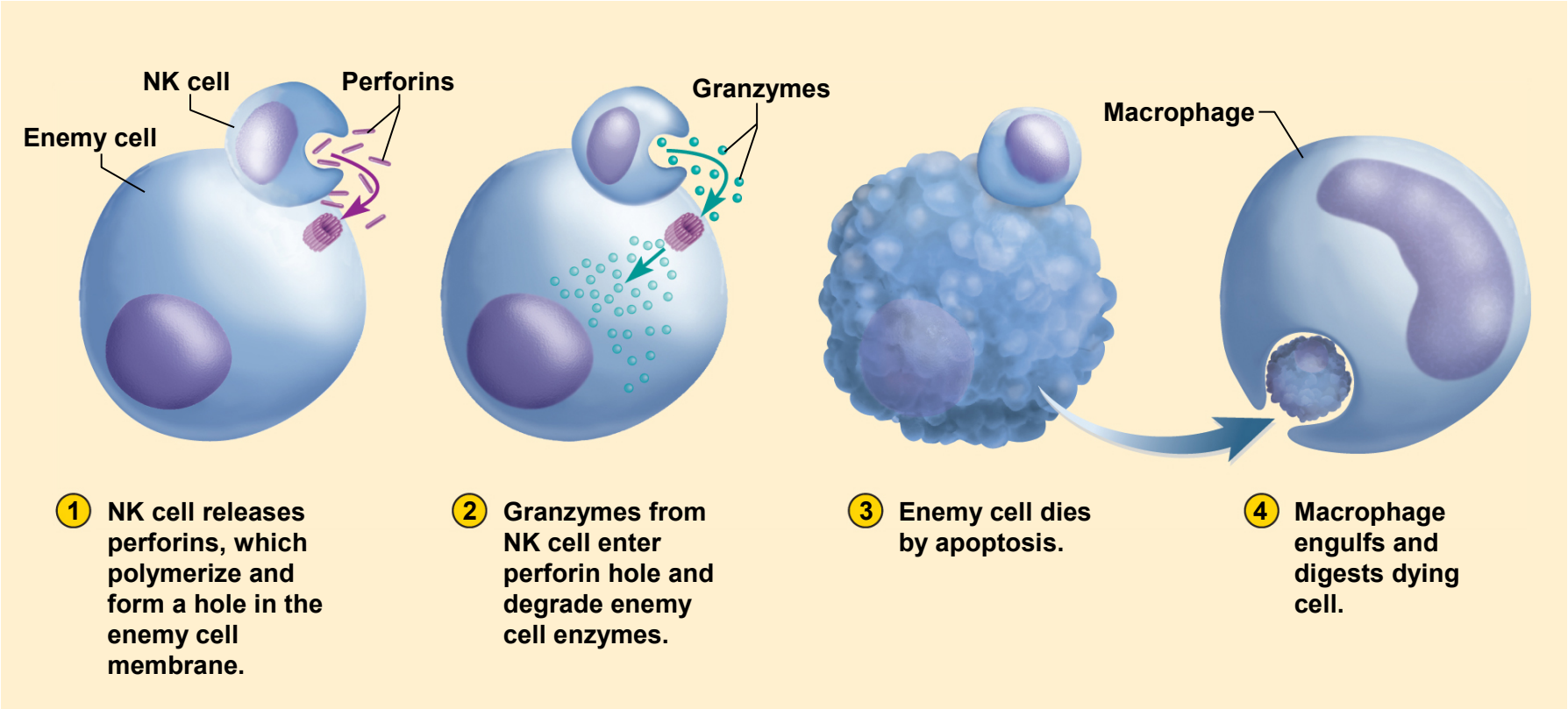


Figure 21.17

Specific Immunity

- **specificity** – immunity directed against a particular pathogen
  - **memory** – when re-exposed to the same pathogen, the body reacts so quickly that there is no noticeable illness

- **two types of immunity**
  - **cellular (cell-mediated) immunity**: (T cells)
    - lymphocytes directly attack and destroy foreign cells or diseased host cells
    - means of ridding the body of pathogens that reside inside human cells, where they are inaccessible to antibodies
    - kills cells that harbor them
  - **humoral (antibody-mediated) immunity**: (B cells)
    - mediated by antibodies that do not directly destroy a pathogen
    - indirect attack where antibodies assault the pathogen
    - can only work against the extracellular stage of infectious microorganisms

Antigens

- **antigen** – any molecule that triggers an immune response

- complex molecules with structures unique to the individual
  - proteins, polysaccharides, glycoproteins, glycolipids
  - can distinguish ‘self’ molecules from foreign

- **epitopes** (antigenic determinants) – certain regions of an antigen molecule that stimulate immune responses

MHC

- Major histocompatability complex
  - Proteins found on cell surface to identify self
  - Unique to the individual
  - MHC I found on all nucleated cells
  - MHC IIfound on antigen presenting cells (APC)

APC's

- Antigen presenting cells
  - Process antigens from the surface of pathogens and present them on the surface adjacent to MHC II

Life Cycle of T cells

- involves three stages and three anatomical stations in the body
- released into the blood from bone marrow as still-undifferentiated stem cells that colonize the thymus
- **mature** in thymus
  - T cells develop **surface antigen receptors**
  - with receptors in place, the T cells are now **immunocompetent** – capable of recognizing antigens presented to them by APCs
  - reticuloendothelial cells in the thymus test T cells by presenting **'self' antigens** to them
  - two ways to fail the test:
    - inability to recognize the RE cells, especially their MHC antigens
      - would be incapable of recognizing a foreign attack on the body
    - reacting to the self antigen
      - T cells would attack one's own tissues

Life Cycle of T cells

- **negative selection** - T cells that fail either test must be eliminated

- negative selection leaves the body in a state of **self-tolerance** in which the surviving T cells respond only to foreign antigens, and tolerating our own
- move to thymus medulla and undergo **positive selection** – they multiply and form **clones** of identical T cells programmed to respond to a specific antigen

- deployment
  - naïve T cells leave thymus and colonize lymphatic tissues and organs everywhere in the body

B Lymphocytes (B cells)

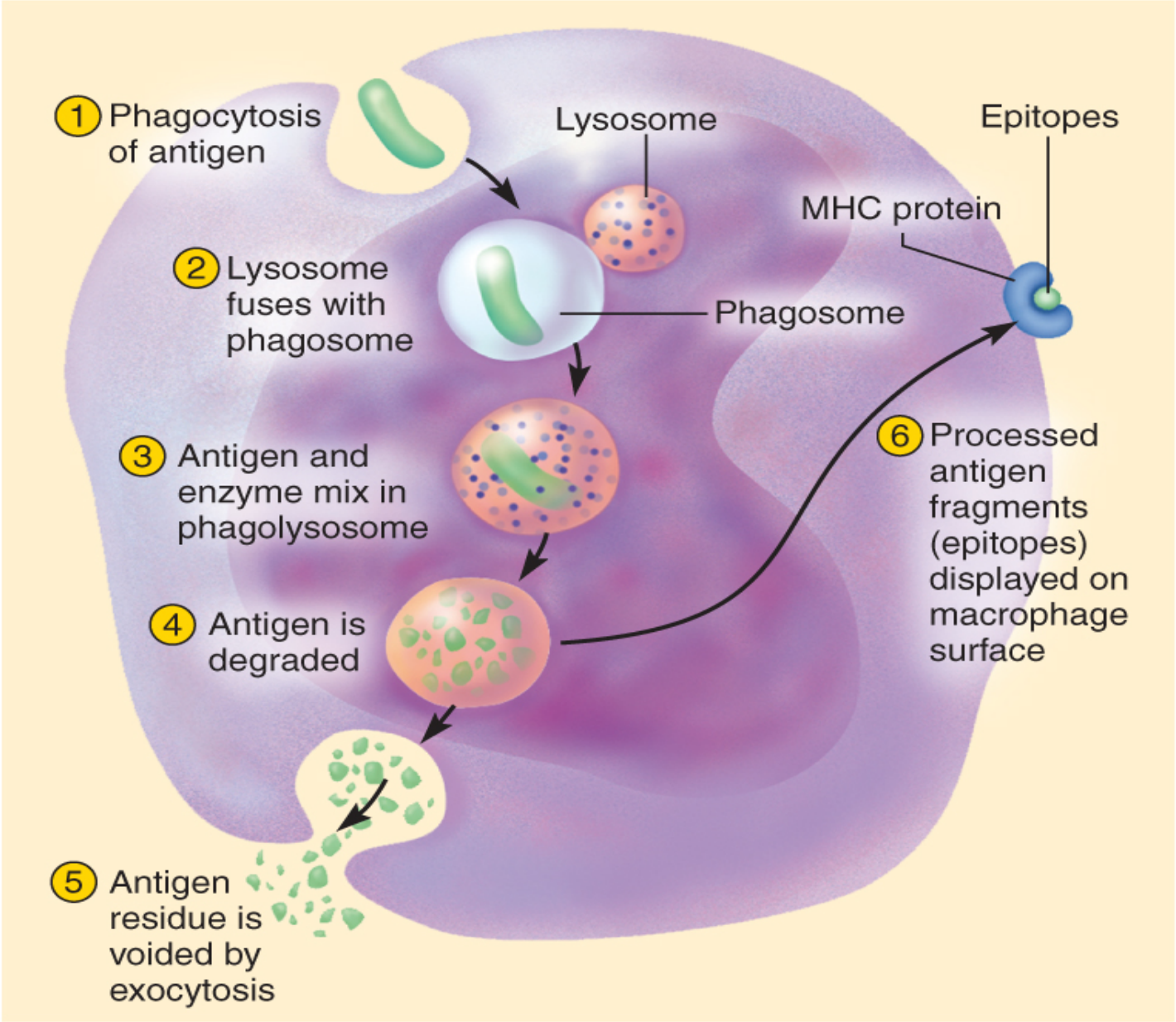
- site of development
  - **bone marrow**
- B cell selection
  - B cells that react to self antigens undergo negative selection same as T cell selection
- **self-tolerant B cells** synthesize antigen surface receptors, divide rapidly, produce immunocompetent clones
- leave bone marrow and colonize same lymphatic tissues and organs as T cells

Antigen-Presenting Cells (APCs)

- T cells can not recognize their antigens on their own
- **antigen-presenting cells** (APCs) are required to help
  - dendritic cells, macrophages, reticular cells, and B cells function as APCs
- function of APCs depends on **major histocompatibility complex (MHC) proteins**
  - act as cell 'identification tags' that label every cell of your body as belonging to you
  - structurally unique for each individual, except for identical twins
- **antigen processing**
  - APC encounters antigen
  - internalizes it by endocytosis
  - digests it into molecular fragments
  - displays relevant fragments (**epitopes**) in the grooves of the MHC protein

Antigen-Presenting Cells (APCs)

- **antigen presenting**
  - **wandering T cells** inspect APCs for displayed antigens
  - if APC only displays a self-antigen, the T cell disregards it
  - if APC displays a nonself-antigen, the T cell initiates an immune attack
  - APCs alert the immune system to the presence of foreign antigen
  - key to successful defense is to quickly mobilize immune cells against the antigen
  - with so many cell types involved in immunity, they require chemical messengers to coordinate their activities – **interleukins**
    - chemical signals from one leukocyte to another



(a)

Cellular Immunity

- **cellular (cell-mediated) immunity** – a form of specific defense in which the **T lymphocytes** directly attack and destroy diseased or foreign cells, and the immune system **remembers** the antigens and prevents them from causing disease in the future

Cellular Immunity

- cellular immunity involves four classes of T cells
  - **cytotoxic T (T_C) cells –** killer T cells
    - the 'effectors' of cellular immunity
    - carry out attack on enemy cells
  - **helper T (T_H) cells**
    - help promote T_C cell and B cell action and nonspecific resistance
  - **regulatory T (T_R) cells – T-regs**
    - inhibit multiplication and cytokine secretion by other T cells
    - limit immune response
  - **memory (T_M) cells**
    - descend from the cytotoxic T cells
    - responsible for memory in cellular immunity

Immunity

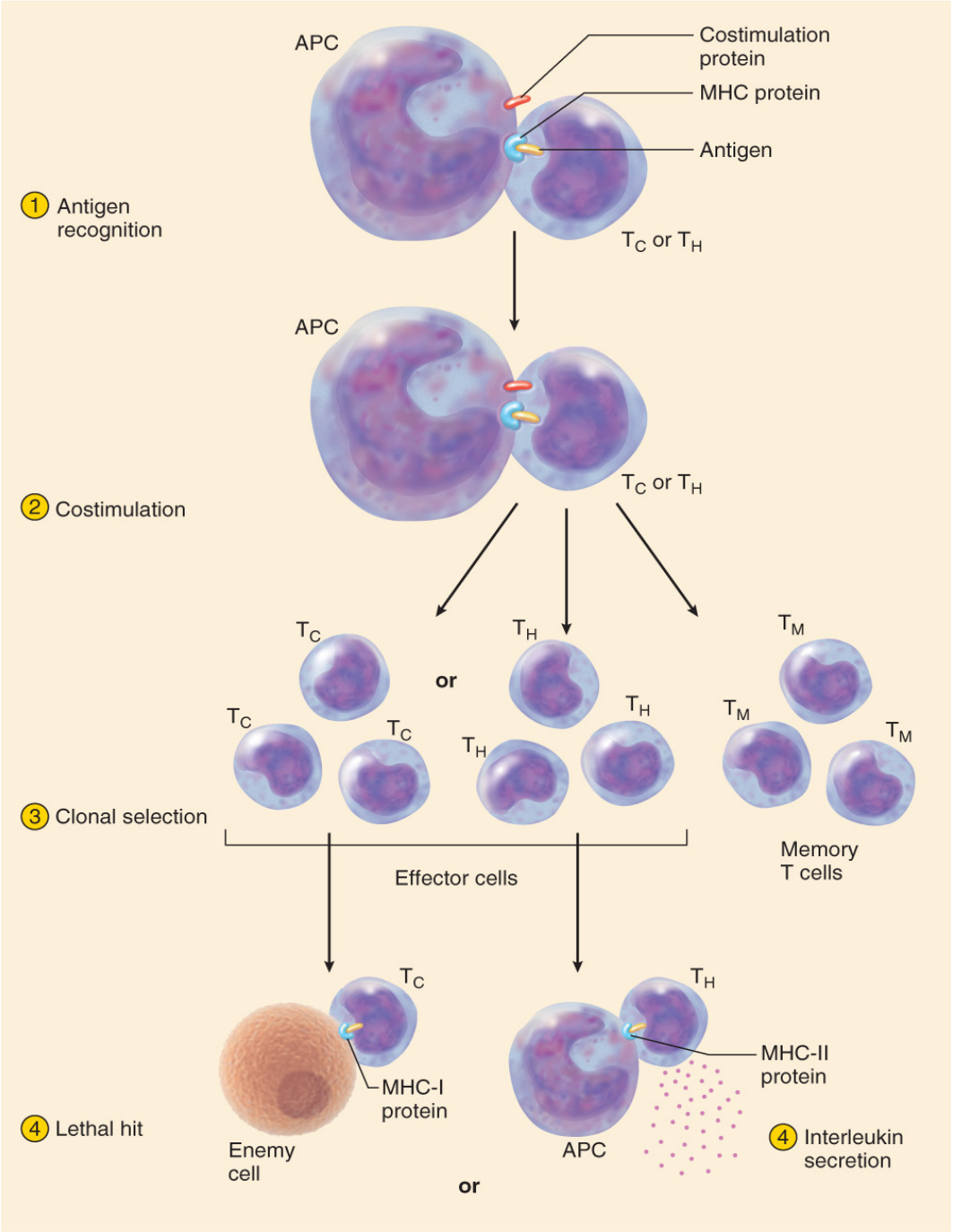
- both cellular and humoral immunity occur in three stages:
  - **recognition**
  - **attack**
  - **memory**
- thought of as the '**three Rs of immunity**'
  - **recognize**
  - **react**
  - **remember**

T Cell Recognition

- **antigen presentation**
  - APC encounters and processes an antigen
  - migrates to nearest lymph node
  - displays it to the T cells
  - when T cell encounters its displayed antigen on the MHC protein, they initiate the immune response
  - T cells respond to **two classes of MHC proteins**
    - **MHC – I proteins**
      - occur on every nucleated cells in the body
    - **MHC – II proteins** (human leukocyte antigens – HLAs)
      - occur only on APCs and display only foreign antigens
  - T_C cells respond only to MHC – I proteins
  - T_H cells respond only to MHC – II proteins

T Cell Recognition

- **T cell activation**
  - begins when T_C or T_H cell binds to a MHCP displaying an epitope that the T cell is programmed to recognize
  - T cell must then bind to another APC protein related to the interleukins
  - T cell must check twice to see if it is really bound to a foreign antigen – **costimulation**
    - helps insure the immune system does not launch an attack in the absence of an enemy
    - would turn against one's own body and injury our tissues
  - successful **costimulation** will trigger **clonal selection**
    - activated T cell undergoes repeated mitosis
    - gives rise to a clone of identical T cells programmed against the same epitope
    - some cells of the clone become **effector cells** and carry out the attack
    - other cells become **memory cells**



Attack : Role of Helper T (T_H) Cells

- **helper T cell** necessary for most immune responses
- play central role in coordinating both cellular and humoral immunity
- when helper T cell **recognizes** the Ag-MHCP complex:
  - **secrete interleukins** that exert three effects:
    - attract neutrophils and NK cells
    - attract macrophages, stimulate their phagocytic activity, and inhibit them from leaving the area
    - stimulate T and B cell mitosis and maturation

Attack : Role of Helper T (T_H) Cells

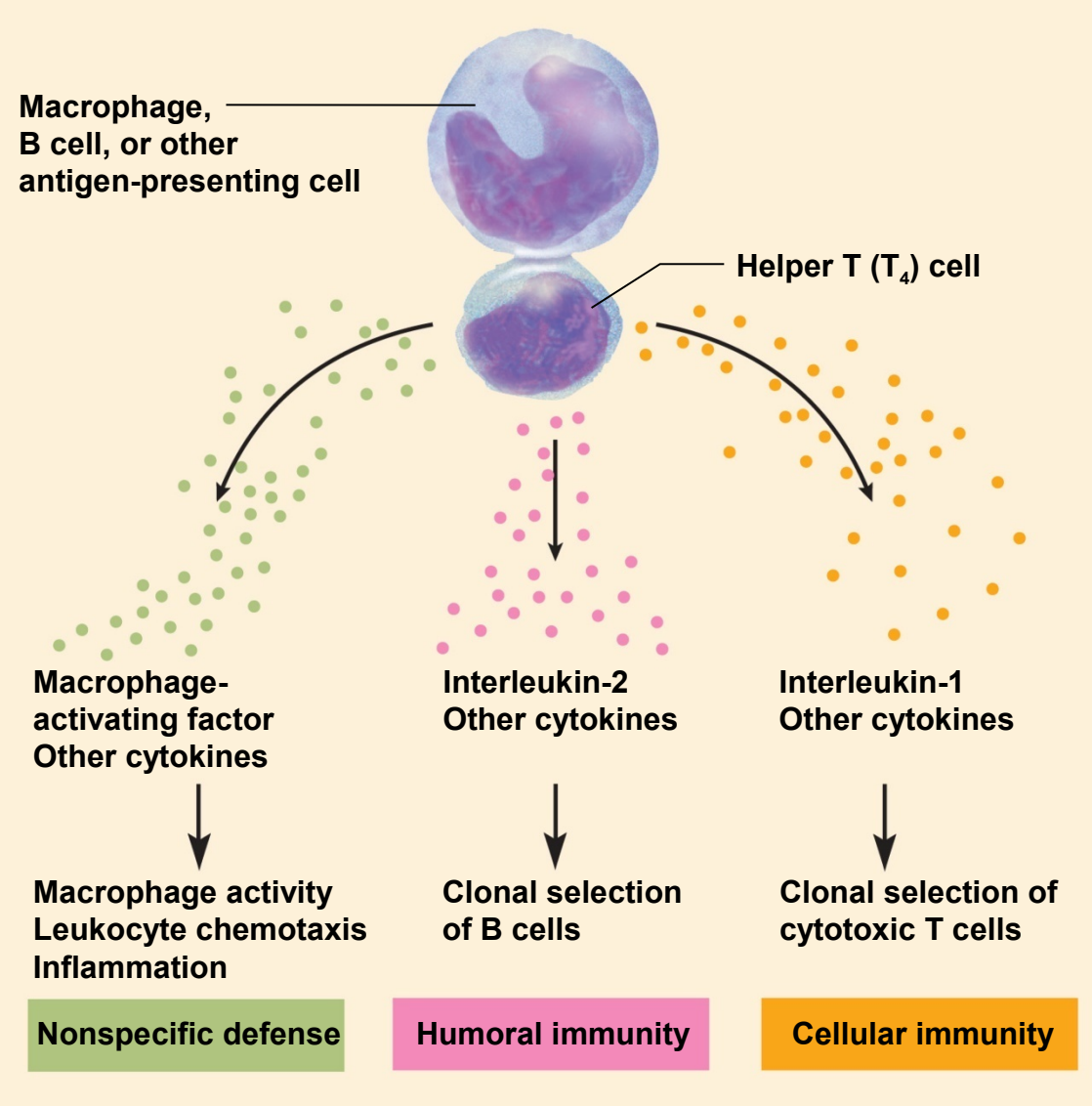
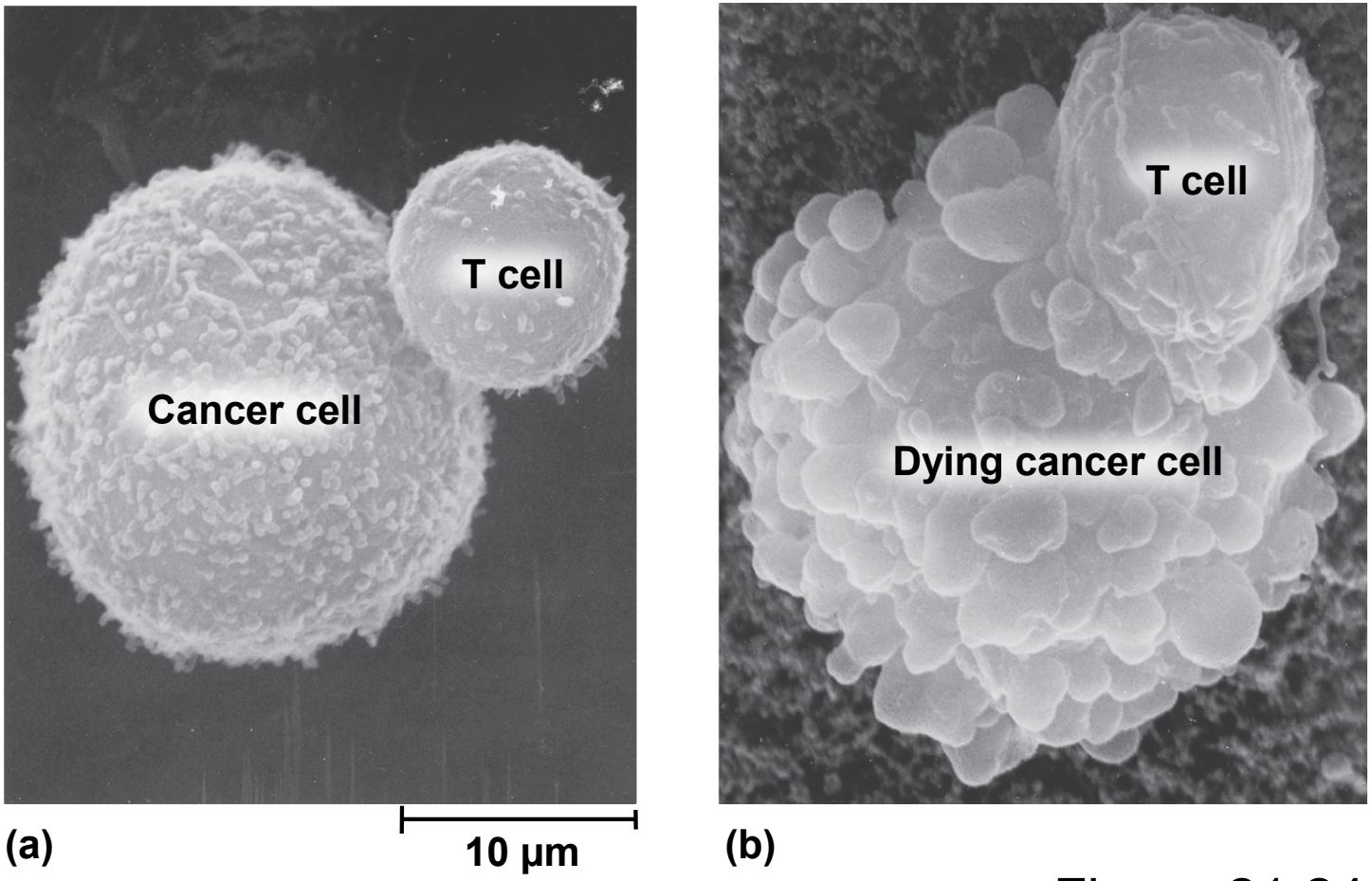


Figure 21.23

Attack : Cytotoxic T (T_c) Cells

- **cytotoxic T (T_c) cell** are the only T cells directly attack other cells
- when T_C cell recognizes a complex of antigen and MHC – I protein on a diseased or foreign cell it 'docks' on that cell
  - delivers a **lethal hit** of toxic chemicals
    - **perforin** and **granzymes** – kill cells in the same manner as NK cells
    - **interferons** – inhibit viral replication
      - recruit and activate macrophages
    - **tumor necrosis factor** (TNF) – aids in macrophage activation and kills cancer cells
  - goes off in search of another enemy cell while the chemicals do their work

Cytotoxic T Cell Function



Dr. Andrejs Liepins

Figure 21.24 a-b

- cytotoxic T cell binding to cancer cell

Memory

- **immune memory** follows primary response
- following clonal selection, some T_C and T_H cells become **memory cells**
  - long-lived
  - more numerous than naïve T cells
  - fewer steps to be activated, so they respond more rapidly
- **T cell recall response**
  - upon re-exposure to same pathogen later in life, memory cells launch a quick attack so that no noticeable illness occurs
  - the person is immune to the disease

Humoral Immunity

- humoral immunity is a more **indirect method** of defense than cellular immunity
- **B lymphocytes** of humoral immunity produce **antibodies** that bind to antigens and tag them for destruction by other means
  - cellular immunity attacks the enemy cells directly
- works in three stages like cellular immunity
  - **recognition**
  - **attack**
  - **memory**

Humoral Immunity

- **recognition**
  - **immunocompetent B** cell has **thousands of surface receptors** for one antigen
  - **activation** begins when an antigen binds to several of these receptors
    - links them together
    - taken into the cell by **receptor-mediated endocytosis**
    - small molecules are not antigenic because they cannot link multiple receptors together
    - **B cell processes** (digests) the antigen
    - links some of the **epitopes** to its MHC–II proteins
    - displays these on the cell surface
  - usually B cell response goes no further unless a **helper T cell** binds to this Ag-MHCP complex
    - bound T_H cell **secretes interleukins** that activate B cell

Humoral Immunity

- **recognition**
  - triggers **clonal selection**
    - **B cell mitosis** gives rise to an entire battalion of identical B cells programmed against the same antigen
    - most **differentiate** into **plasma cells**
    - larger than B cells and contain an abundance of **rough ER**
    - secrete antibodies at a rate of 2,000 molecules per second during their life span of 4 to 5 days
    - antibodies travel through the body in the blood or other body fluids
      - first exposure antibodies **IgM**, later exposures to the same antigen, **IgG**
- **attack**
  - antibodies bind to antigen, render it harmless, ‘tag it’ for destruction
- **memory**
  - some B cells differentiate into **memory cells**

Humoral Immunity - Recognition

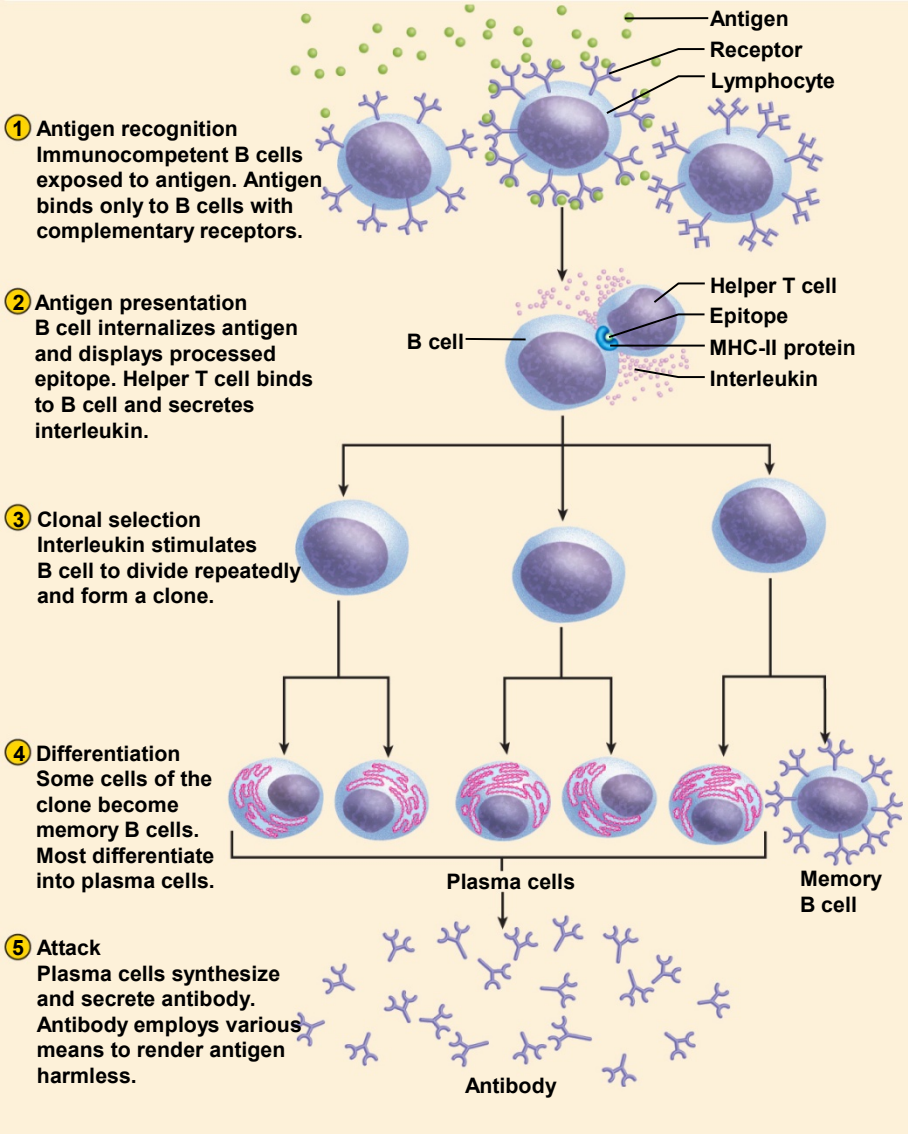
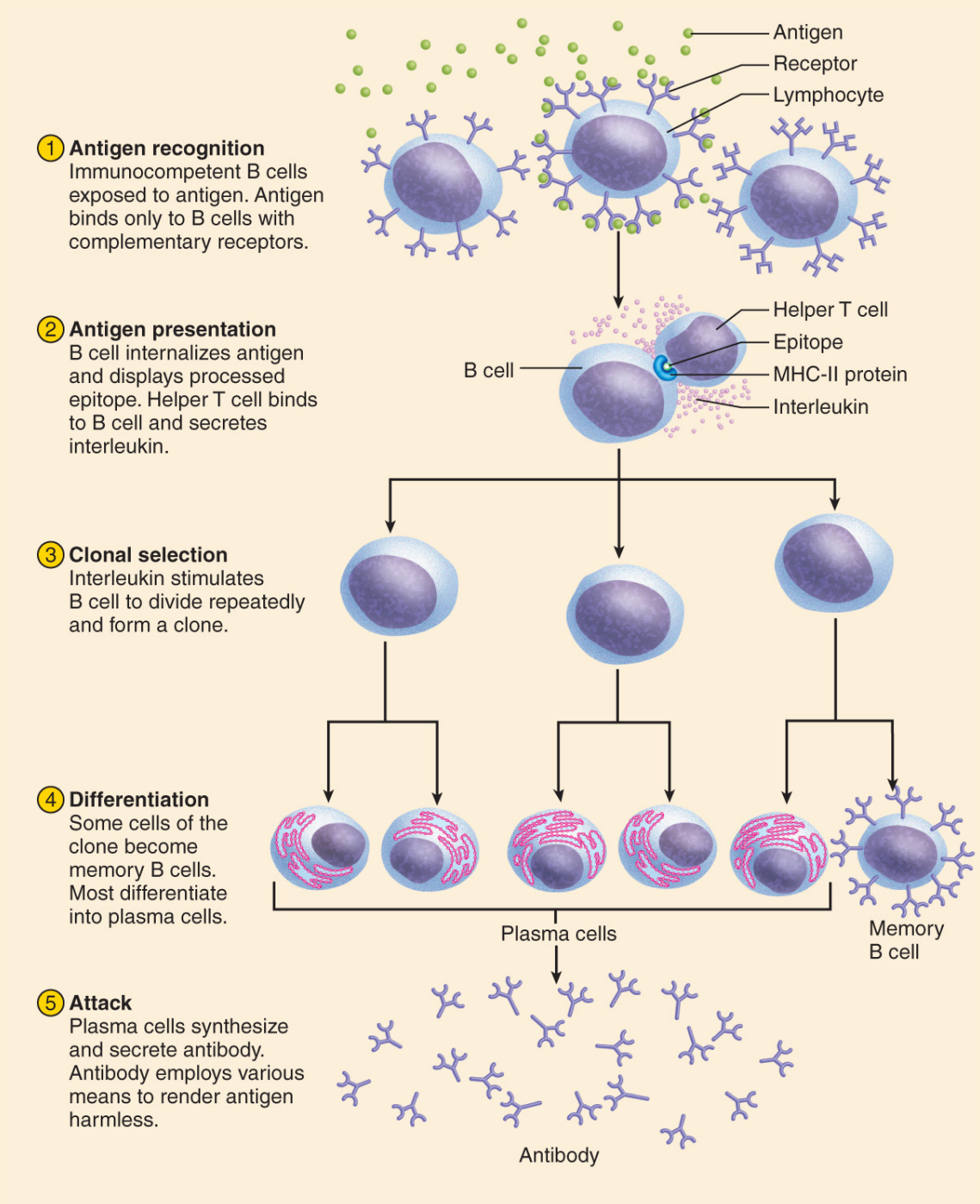
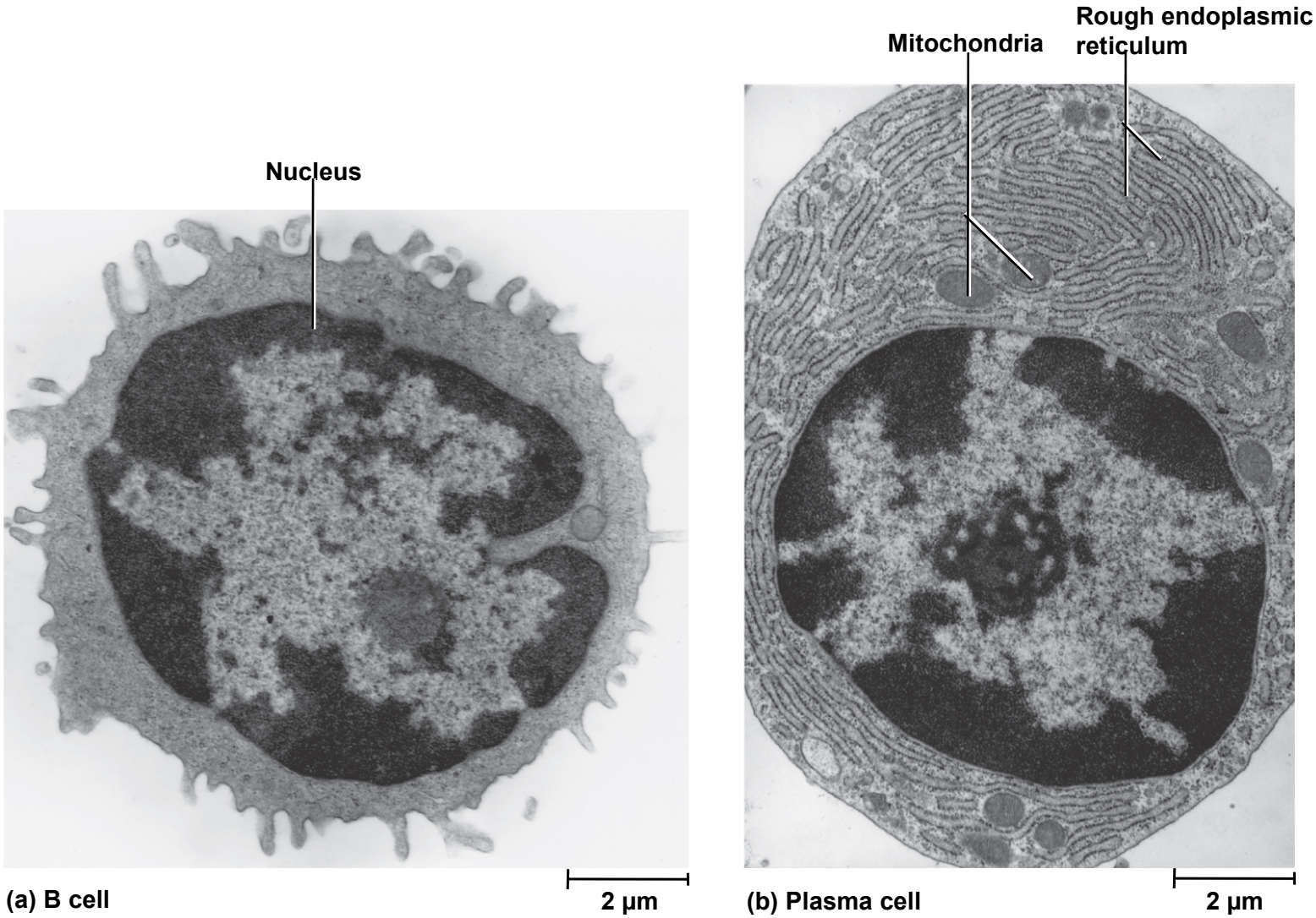


Figure 21.25



B cells and Plasma cells



(a) B cell

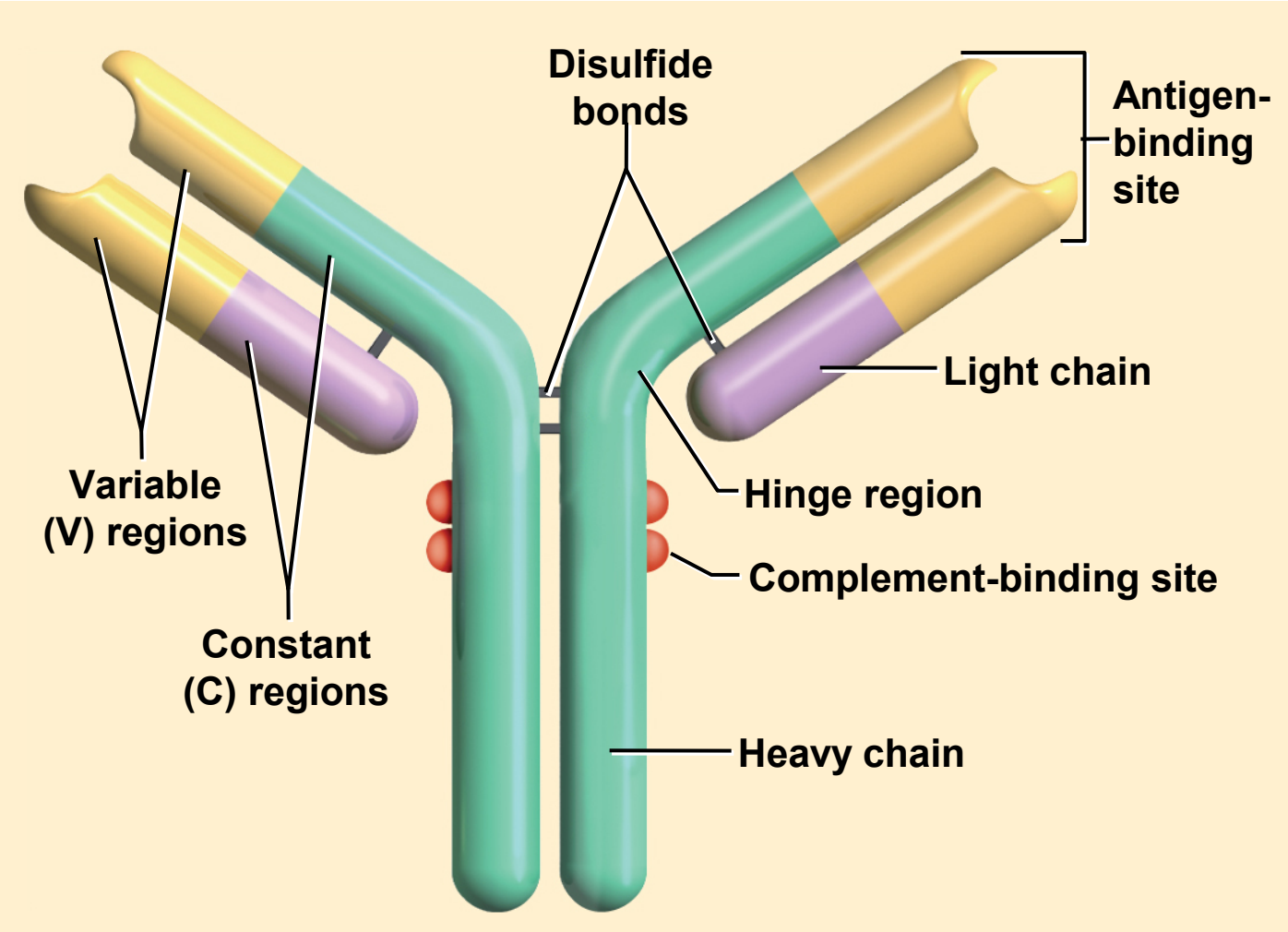
(b) Plasma cell

Figure 21.26 a-b

Antibodies

- **immunoglobulin (Ig)** – an **antibody** is a defensive gamma globulin found in the blood plasma, tissue fluids, body secretions, and some leukocyte membranes
- **antibody monomer** – the basic structural unit of an antibody
  - composed of four polypeptide chains linked by **disulfide (-S-S-) bonds**
  - two larger **heavy chains** about 400 amino acids long
    - heavy chains have a hinge region where antibody is bent
  - two **light chains** about half as long
  - **variable (V) region** in all four chains
    - gives the antibody its uniqueness
  - **antigen binding site** – formed from the V regions of the heavy and light chain on each arm
    - attaches to the epitope of an antigen molecule
  - **constant (C) region** has the same amino acid sequence within one person and determines mechanism of antibody action

Antibody Structure



(a)

Figure 21.27a

Five Classes of Antibodies

- named for the structure of their C region
  - **IgA -** monomer in plasma; dimer in mucus, saliva, tears, milk, and intestinal secretions
    - prevents pathogen adherence to epithelia and penetrating underlying tissues
    - provides passive immunity to newborns
  - **IgD -** monomer; B cell transmembrane antigen receptor
    - thought to function in B cell activation by antigens
  - **IgE -** monomer; transmembrane protein on basophils and mast cells
    - stimulates release of histamine and other chemical mediators of inflammation and allergy
      - attracts eosinophils to parasitic infections
      - produces immediate hypersensitivity reactions
  - **IgG -** monomer; constitutes 80% of circulating antibodies
    - crosses placenta to fetus, secreted in secondary immune response, complement fixation
  - **IgM** – pentamer in plasma and lymph
    - secreted in primary immune response, agglutination, complement fixation

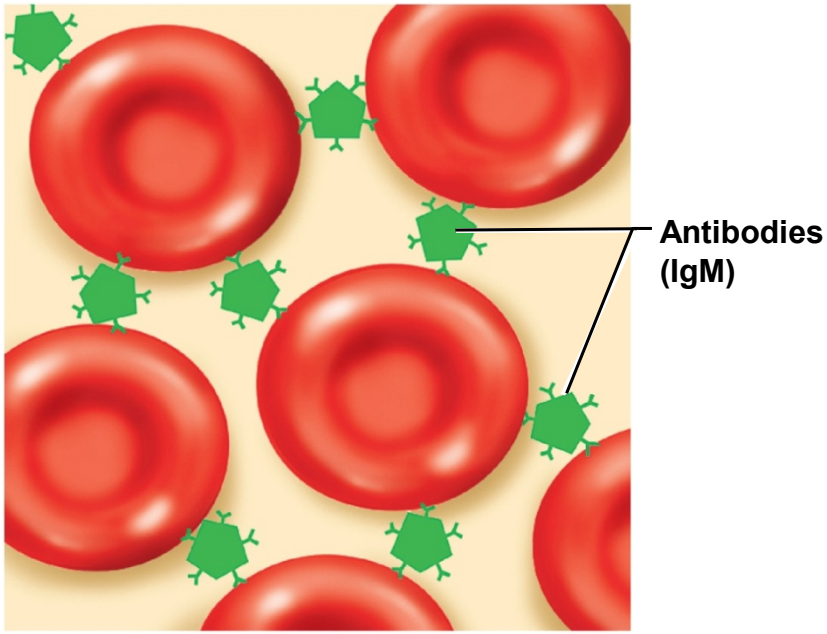
Antibody Diversity

- human immune system capable of as many as 1 trillion different antibodies
- 35,000 genes in human genome
- **somatic recombination**
  - DNA segments shuffled and form new combinations of base sequences to produce antibody genes
- **somatic hypermutation**
  - B cells in lymph nodules rapidly mutate creating new sequences

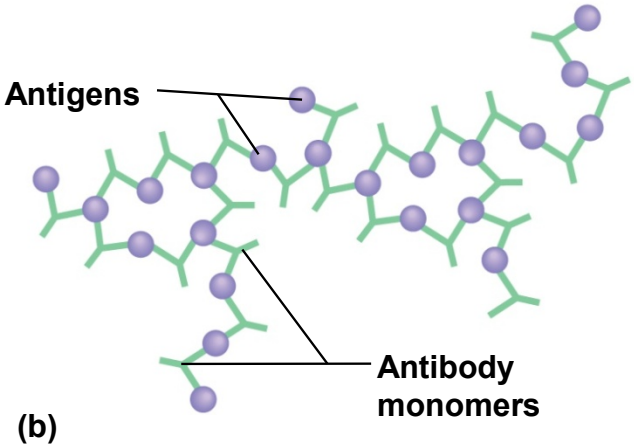
Humoral Immunity - Attack

- **neutralization**
  - antibodies mask pathogenic region of antigen
- **complement fixation**
  - antigen binds to IgM or IgG, antibody changes shape, initiates complement binding which leads to inflammation, phagocytosis, immune clearance, or cytolysis
  - primary defense against foreign cells, bacteria, and mismatched RBCs
- **agglutination**
  - antibody has 2-10 binding sites; binds to multiple enemy cells immobilizing them from spreading
- **precipitation**
  - antibody binds antigen molecules (not cells); creates antigen-antibody complex that precipitates, phagocytized by eosinophils

Agglutination and Precipitation



(a)



(b)

Figure 21.28 a-b

Humoral Immunity - Memory

- **primary immune response** – immune reaction brought about by the first exposure to an antigen
  - appearance of protective antibodies delayed for 3 to 6 days while naïve B cells multiply and differentiate into plasma cells
  - as plasma cells produce antibodies, the **antibody titer** (level in the blood plasma) rises
  - primary response leaves one with an immune memory of the antigen

Humoral Immunity - Memory

- **Secondary response** – if re-exposed to the same antigen
  - plasma cells form within hours
  - IgG titer rises sharply and peaks in a few days
  - response is so rapid that the antigen has little chance to exert a noticeable effect on the body
  - no illness results
  - low levels of IgM also secreted and quickly declines
  - IgG remain elevated for weeks to years
    - conferring long lasting protection
    - memory does not last as long in humoral immunity as in cellular immunity

Humoral Immunity Responses

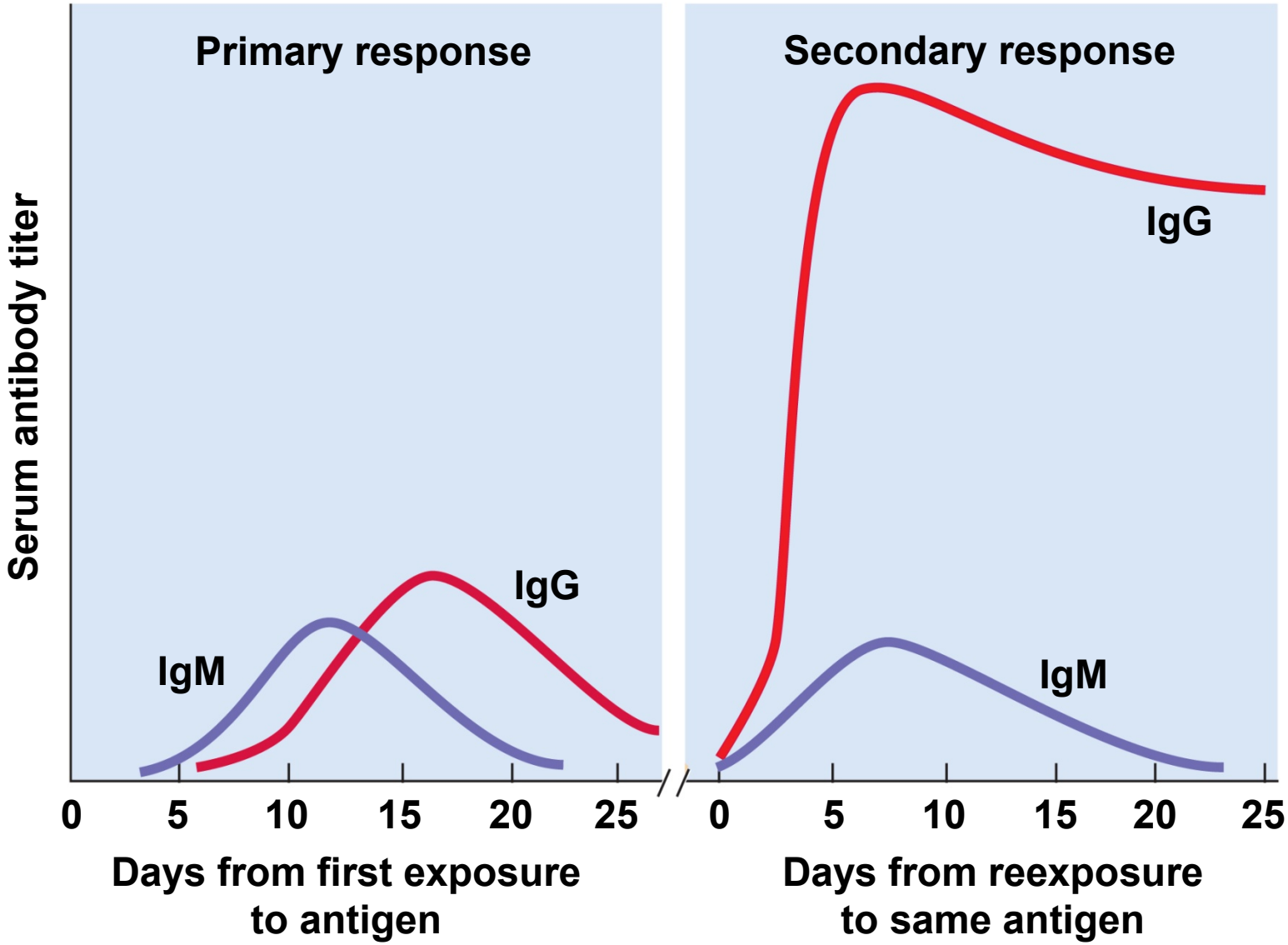


Figure 21.29

Immune System Disorders

- immune response may be:
  - **too vigorous**
  - **too weak**
  - **misdirected against wrong targets**

Hypersensitivity

- **hypersensitivity** – an excessive immune reaction against antigens that most people tolerate
- includes:
  - **alloimmunity** - reaction to transplanted tissue from another person
  - **autoimmunity** - abnormal reactions to one's own tissues
  - **allergies** – reactions to environmental antigens (**allergens**) – dust, mold, pollen, vaccines, bee and wasp venom, poison ivy and other plants, foods such as nuts, milk, eggs, and shellfish, drugs such as penicillin, tetracycline, and insulin

Autoimmune Diseases

- **autoimmune diseases** - failures of self-tolerance
- immune system fails to distinguish self-antigens from foreign ones
  - produces **autoantibodies** that attack the body's own tissues
- three reasons why self-tolerance
  - **cross-reactivity**
    - some antibodies against foreign antigens react to similar self-antigens
    - rheumatic fever - streptococcus antibodies also react with heart valves
  - **abnormal exposure of self-antigens in the blood**
    - some of our native antigens are not exposed to blood
    - blood-testes barrier isolates sperm from blood
  - **changes in structure of self-antigens**
    - viruses and drugs may change the structure of self-antigens or cause the immune system to perceive them as foreign
- **self-reactive T cells**
  - not all are eliminated in thymus and are normally kept in check by regulatory T (T_R) cells

Immunodeficiency Diseases

- immune system fails to react vigorously enough
- **Severe Combined Immunodeficiency Disease (SCID)**
  - hereditary lack of T and B cells
  - vulnerability to opportunistic infection and must live in protective enclosures

Figure 21.30

Immunodeficiency Diseases

- **Acquired Immunodeficiency Syndrome (AIDS)** – nonhereditary diseases contracted after birth
- group of conditions that involve and **severely depress the immune response**
- caused by infection with the **human immunodeficiency virus (HIV)**
  - HIV structure *(next slide)*
  - invades helper T cells, macrophages and dendritic cells by "tricking" them to internalize viruses by receptor mediated endocytosis
  - *re*verse *tr*anscriptase (*retro*virus) uses viral RNA as template to synthesize DNA
    - new DNA inserted into host cell DNA (may be dormant for months to years)
    - when activated, it induces the host cell to produce new viral RNA, capsid proteins, and matrix proteins
    - they are coated with bits of the host cell's plasma membrane
    - adhere to new host cells and repeat the process

HIV Structure

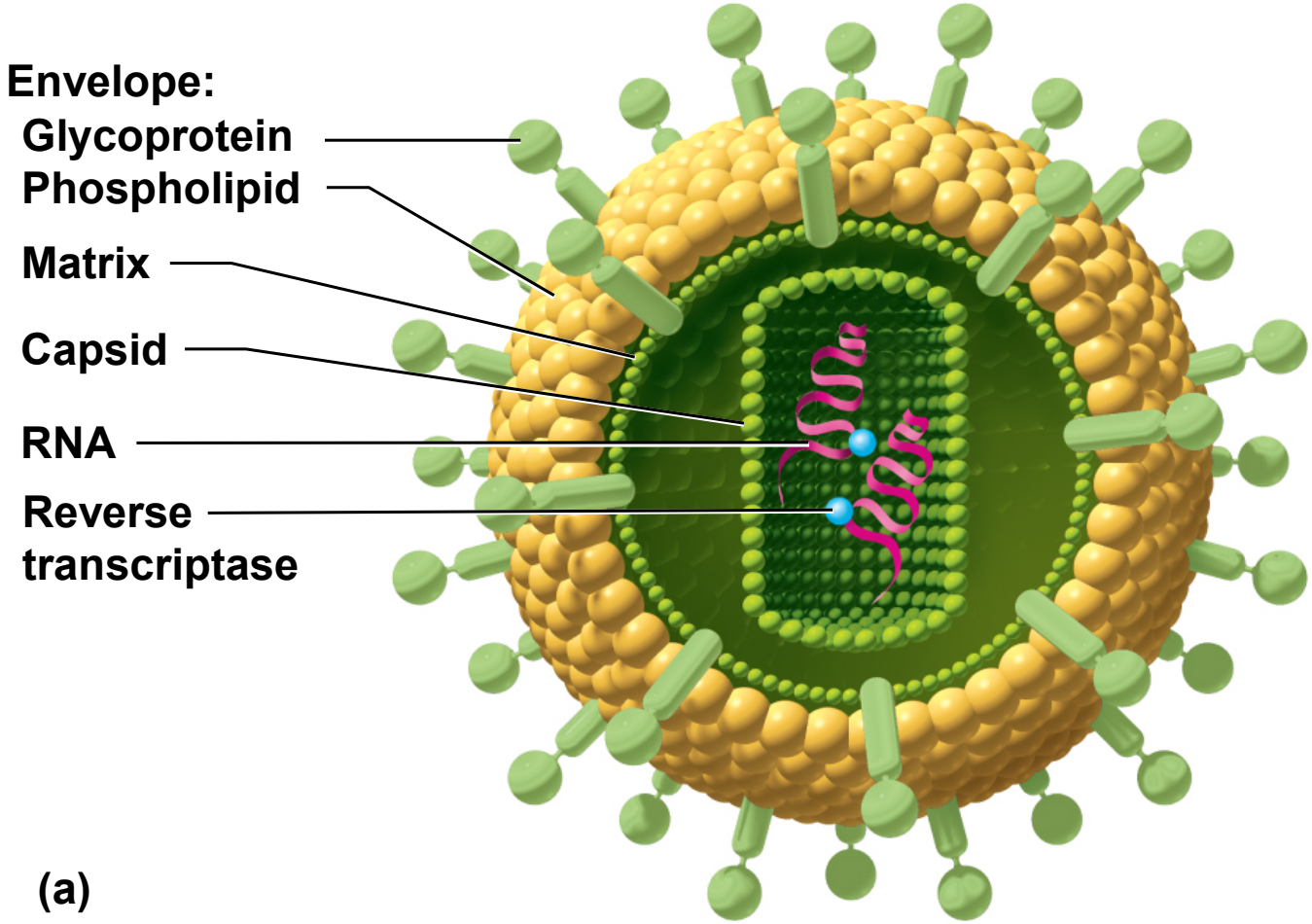


Figure 21.31a

AIDS

- by destroying T_H cells, HIV strikes at the central coordinating agent of nonspecific defense, humoral immunity, and cellular immunity
- incubation period ranges from several months to 12 years

Treatment Strategies

- prevent binding to CD4 proteins of T_H cells
- disrupt reverse transcriptase to inhibit assembly of new viruses or their release from host cells
- medications
  - none can eliminate HIV, all have serious side-effects
  - HIV develops drug resistance
    - medicines used in combination
  - AZT (azidothymidine)
    - first anti-HIV drug - inhibits reverse transcriptase
  - protease inhibitors
    - inhibit enzymes HIV needs to replicate
  - now more than 24 anti-HIV drugs on the market