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
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

Figure 21.3b

Lymph
Opening
Tissue fluid
Endothelium of lymphatic capillary
Anchoring filaments

Figure 21.3b
Valve in a Lymphatic Vessel

Figure 21.4a

(a) Valve

Figure 21.4b

(b) Lymph flows forward through open valves

Lymph

Closed valves prevent backflow
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
Lymphatic system

- Lymphatic capillaries
- Lymph nodes
- Lymphatic trunks
- Collecting duct
- Collecting vessels
- Lymph flow

Cardiovascular system

- Pulmonary circuit
- Subclavian vein
- Superior vena cava
- Blood flow
- Systemic circuit

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
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

Intestinal villus

Lymphatic nodule

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
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

Diaphragm
Spleen
Splenic artery
Splenic vein
Pancreas
Kidney
Inferior vena cava
Aorta
Common iliac arteries

(a)

Inferior vena cava
Common iliac arteries

Figure 21.14b

Spleen
Gastric area
Hilum
Renal area
Splenic vein
Splenic artery

(b)

Superior

Figure 21.14c

Red pulp
Central artery (branching)
White pulp

(c)
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

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$_2^-$, H$_2$O$_2$)
  – 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

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
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**

1. **NK cell** releases perforins, which polymerize and form a hole in the enemy cell membrane.
2. **Granzymes** from NK cell enter perforin hole and degrade enemy cell enzymes.
3. **Enemy cell** dies by apoptosis.
4. **Macrophage** engulfs and digests dying cell.

---

**Figure 21.17**

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
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 histocompatibility complex
  - Proteins found on cell surface to identify self
  - Unique to the individual
  - MHC I found on all nucleated cells
  - MHC II found 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
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<sub>c</sub>) cells – killer T cells
    - the ‘effectors’ of cellular immunity
    - carry out attack on enemy cells
  - **helper T** (T<sub>H</sub>) cells
    - help promote T<sub>c</sub> cell and B cell action and nonspecific resistance
  - **regulatory T** (T<sub>R</sub>) cells – T-regs
    - inhibit multiplication and cytokine secretion by other T cells
    - limit immune response
  - **memory** (T<sub>M</sub>) 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\textsubscript{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 (T₄) Cells

Figure 21.23

Macrophage, B cell, or other antigen-presenting cell

Helper T (T₄) cell

Macrophage-activating factor
Other cytokines

Interleukin-2
Other cytokines

Interleukin-1
Other cytokines

Macrophage activity
Leukocyte chemotaxis
Inflammation

Clonal selection of B cells

Clonal selection of cytotoxic T cells

Nonspecific defense
Humoral immunity
Cellular immunity

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
Attack: Cytotoxic T (T\textsubscript{C}) Cells

- **cytotoxic T (T\textsubscript{C}) cell** are the only T cells directly attack other cells
- when T\textsubscript{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

- cytotoxic T cell binding to cancer cell

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

Figure 21.24 a-b

Dr. Andrejs Liepins
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

1. Antigen recognition
   Immunocompetent B cells exposed to antigen. Antigen binds only to B cells with complementary receptors.

2. Antigen presentation
   B cell internalizes antigen and displays processed epitope. Helper T cell binds to B cell and secretes interleukin.

3. Clonal selection
   Interleukin stimulates B cell to divide repeatedly and form a clone.

4. Differentiation
   Some cells of the clone become memory B cells. Most differentiate into plasma cells.

5. Attack
   Plasma cells synthesize and secrete antibody. Antibody employs various means to render antigen harmless.
1. **Antigen recognition**
   Immunocompetent B cells exposed to antigen. Antigen binds only to B cells with complementary receptors.

2. **Antigen presentation**
   B cell internalizes antigen and displays processed epitope. Helper T cell binds to B cell and secretes interleukin.

3. **Clonal selection**
   Interleukin stimulates B cell to divide repeatedly and form a clone.

4. **Differentiation**
   Some cells of the clone become memory B cells. Most differentiate into plasma cells.

5. **Attack**
   Plasma cells synthesize and secrete antibody. Antibody employs various means to render antigen harmless.
B cells and Plasma cells

Figure 21.26 a-b

(a) B cell

(b) Plasma cell

Nucleus

Mitochondria

Rough endoplasmic reticulum

2 µm

2 µm

© Dr. Don W. Fawcett/Visuals Unlimited
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

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

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

Primary response

Secondary response

Days from first exposure to antigen

Days from reexposure to same antigen

Serum antibody titer

IgM

IgG

IgG

IgM
Immune System Disorders

• immune response may be:
  – too vigorous
  – too weak
  – misdirected against wrong targets
Hypersensitivity

• **hypo-sensitivity** – an excessive immune reaction against antigens that most people tolerate

• includes:
  - **allo-immunity** - reaction to transplanted tissue from another person
  - **auto-immunity** - 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\textsubscript{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
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
  – reverse transcriptase (retrovirus) 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

Envelope:
Glycoprotein
Phospholipid
Matrix
Capsid
RNA
Reverse transcriptase

(a)

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