

Chapter 15 Outline

- ▶ Defense Mechanisms
- ▶ Functions of B Lymphocytes
- ▶ Functions of T Lymphocytes
- ▶ Active and Passive Immunity
- ▶ Tumor Immunology
- ▶ Diseases Caused By Immune System

15-2

Immune System

Anatomy - Lymphoid tissue:

- 1) Primary tissue: thymus gland & bone marrow
- 2) Secondary tissue: spleen, lymph nodes, tonsils, GALT

Tries to:

- 1) recognize & remove abnormal "self" cells
- 2) removes dead & damaged cells
- 3) protect body from pathogens

▶ Immune system can be grouped into 2 categories:

- ▶ Innate (nonspecific) immunity: general defense guard against wide range of pathogens – don't care what it is
- ▶ Adaptive (specific) immunity is a function of lymphocytes and directed against specific invaders

15-3

Innate (non-specific) Immunity

- ▶ Bodies 1st line of defense against invading pathogens is Physical (skin) & chemical barriers
- ▶ If invaders get past barriers then our innate immunity provides a 2nd line of defense
 - ▶ Distinguishes invader as "non-self"
 - ▶ Uses cells and their chemicals to destroy invader
- ▶ Includes: epithelial barriers, pH of gastric juice, phagocytosis, mucus membranes, interferons, and fever
- ▶ Innate immunity tries to kill outright or contain it until our Acquired (specific) immune system can

15-5

Activation of Innate Immunity

- ▶ Invading pathogens have unique pathogen-associated molecular patterns (PAMPs)
 - Molecules on membrane of pathogens
- ▶ Some immune cells have Toll-like receptors for PAMPs on their surfaces
- ▶ If Dendritic cells, neutrophils macrophages toll-like receptors bind with PAMPs on a bacteria
 - An immune response will be activated:
 - Phagocytosis
 - Complement system activated

15-6

Innate Defense: Phagocytosis

- ▶ 3 major groups of phagocytic cells:
 1. Neutrophils - 1st to arrive at infection sites
 2. Monocytes - macrophages
 3. Organ-specific (fixed) phagocytes in liver, spleen, lymph nodes, lungs, and brain

Phagocytes attracted to Chemotaxins – chemicals released by bacteria or cell wall components

If phagocytes toll-like receptors bind to PAMPs:

1. Phagocytosis occurs
2. Invader ends up in Phagosome
3. Enzymes/oxidizing agents break it down

- ▶ More to come later – Acquired Specific immunity

15-7

Natural Killer (NK) Cells

- ▶ Are lymphocytes
- ▶ Provide first line of cell-mediated defense
- ▶ Part of the innate immune system
- ▶ Detect virus-infected cells and promote apoptosis
- ▶ NK cells destroy tumors in a non-specific fashion
 - ▶ Can secrete interferons – chemicals that interfere with virus replication

15-80

Innate Immunity: Interferons

- ▶ Cytokines produced by cells infected with virus or released by immune cells
- ▶ Non-specific resistance to viral infection in nearby uninfected cells
- ▶ Virus in cell stimulates it to produce interferons
 - Interferons move into neighbor uninfected cells
- ▶ **Block ability of virus to replicate in neighboring cells**
- ▶ Also
 - Stimulate macrophages
 - Stimulate T cells & NK cells
 - Production of antibodies
- ▶ 3 types: alpha, beta, and gamma interferon

15-11

Innate Immunity: Fever

- ▶ Recall hypothalamus regulates our internal temp.
- ▶ In response to toxins released by bacteria or bacterial recognition by monocytes and macrophages
 - ▶ They release cytokines (pyrogens)
 - ▶ Hypothalamic thermostat is reset upwards (fever)
 - ▶ Enhances phagocytosis
 - ▶ Some enzymatic reax for immunity speed up
 - ▶ Limit bacterial activity
- ▶ Increase sleepiness
- ▶ Fe and Zinc removed from plasma (spleen)

15-10

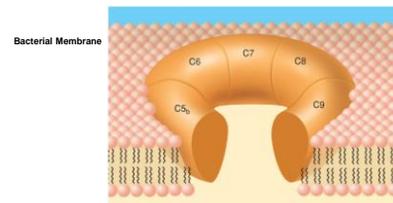
Local Inflammation

- ▶ Starts with an innate defense and can end with an adaptive defense
- ▶ Purpose:
 1. Limit spread of pathogens
 2. remove debris/damaged tissue
 3. initiate repair
- ▶ Occurs when **bacteria** enter a break in the skin
- ▶ Inflammatory reaction is initiated by **nonspecific mechanisms** of 1) phagocytosis and 2) complement activation

15-24

Compliment Proteins

- ▶ Plasma proteins (globulins)
- ▶ Activated by bacteria/virus/pathogen OR Antibodies
 - ▶ Inflation: stimulate basophils/mast cells to release histamine
 - ▶ Coats microorg attracting Phagocytes (opsinization)
 - ▶ Binds pathogen to RBC that take to spleen or liver
 - ▶ Create a membrane attack complex

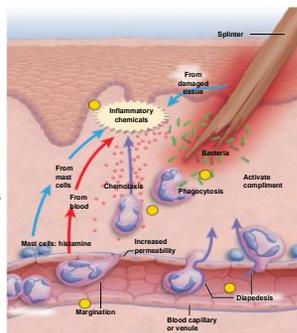


15-41

Local Inflammation

Chemicals from bacteria

1. **Attract macrophages**
 2. **Cause mast cells to release histamine**
- ▶ **Endothelium permeability**
 - ▶ **Neutrophils arrive Release cytokines:**
 - ▶ **Attract neutrophils/macrophages**
 - ▶ **And activate compliment proteins (attracts more macrophages)**



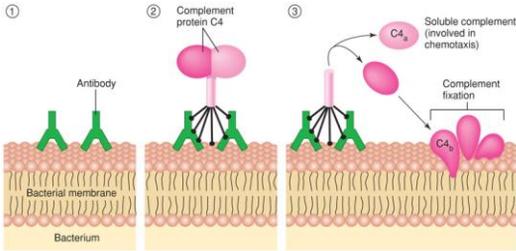
15-27

Local Inflammation – Specific Immunity

- ▶ As inflammation progresses, B cells produce antibodies against bacterial antigens
 - ▶ Antibody attachment to antigens amplifies complement activation
 - ▶ Promotes phagocytic activity of neutrophils, macrophages, and monocytes

15-25

Fixation of Complement Proteins



15-40

15-15

Adaptive (Specific or Acquired) Immunity

- ▶ Acquired ability to defend against specific a pathogen by prior exposure to the pathogen
- ▶ Humeral Immunity: B-cells (antibodies)
- ▶ Cell-mediated Immunity: T-cells (must come in contact)
- Antigens have **antigenic determinants sites** – region of antigen that binds to antibodies
- We have self antigens & our immune system can recognize them

Lymphocytes are involved in Specific Immunity

T-cells and B-cells

- ▶ Both created in bone marrow
- ▶ B-cells: Humeral Immunity
 - ▶ Fight pathogens in fluids of our body
 - ▶ Have antibodies on their surface
 - ▶ To attach to pathogens
 - ▶ Responsible for secretion of Antibodies in response to a pathogen
 - ▶ Activated B-cells can make plasma cells & memory B-cells
- ▶ T-cells: Cell Mediated Immunity
 - mature in the thymus (immunocompitant)
 - ▶ Insert T-cell receptors
 - Do not secrete antibodies
 - Attack host cells infected with virus or fungi, or cancer cells
 - Types include: Helper T cells, Cytotoxic T cells,

15-19

B Lymphocytes (B cells)

- ▶ B-cells have antibodies on membrane that can bind to antigens
- ▶ **ANTIGENS: Any molecules that elicits production of antibodies/or any immune response**
- ▶ B-cells produce anti-bodies (plasma cells)
 - plasma proteins immunoglobulins (or gammaglobulins)
 - specific for a particular antigen
 - 100 million trillion in your body
 - Millions specific for different antigens
 - Each B-cell has specific anti-bodies on its surface
 - Millions just floating about in our fluids
 - Unique structure of 4 polypeptides/with a specific binding site

15-28

Antibody Structure

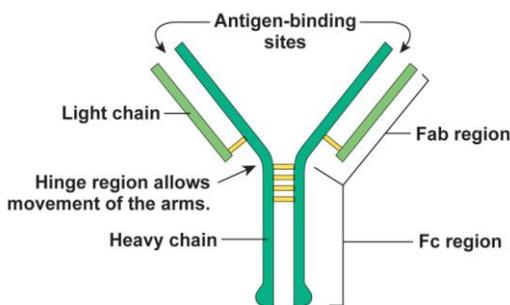


Figure 24-12

Functions of Antibodies

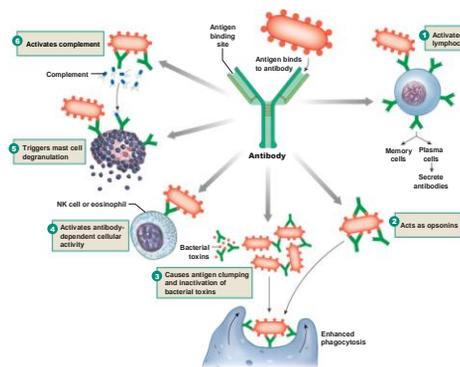
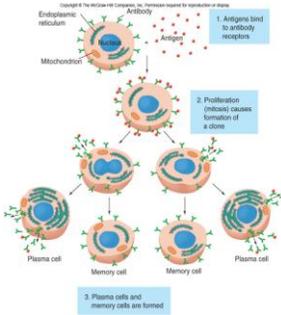


Figure 24-13

B Lymphocytes (B cells)

- ▶ When B cells binds to an antigen it becomes activated
 - ▶ Makes clones
 - ▶ 1. memory B cells
 - ▶ 2. effector cells that turn into plasma cells
- plasma cells: produce antibodies specific for antigen
- Lots of antibodies are made



15-29

T-cells (Helper T-cells & Cytotoxic T-cells)

T-cells attack cells that have a pathogen inside!
Killer (Cytotoxic) T Cells

- ▶ Destroy body cells that possess foreign antigens
 - ▶ Virus/fungus
 - ▶ Cancerous cells
- ▶ Kill by cell-mediated destruction
 - ▶ Must be in contact with victim cell to kill it
 - ▶ Secret perforins - create a pore in victim's membrane and cause lysis
 - ▶ Secrete granzymes which enter cell activate caspases (cause apoptosis)

15-44

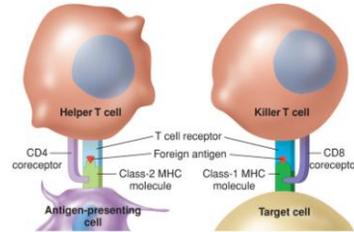
How T cells Become activated

- ▶ **T cell receptors cannot bind to free antigens**
- ▶ T- cells have to be presented an antigen (**antigen-presenting cells**)
- **macrophages & dendritic cells**
 - ▶ Engulf antigens, partially digest them, and display a piece of the antigen on their surface for T cells to "see"
 - ▶ Antigens are presented on the Major Histocompatibility Complex (MHC)
 - Protein complex that displays antigens
 - and T-cell receptor can hook up to it
 - MHCs occur on surfaces of all body cells (except RBCs)
- ▶ T-cells cruise about checking out the MHC proteins

15-47

Major Histocompatibility Complex

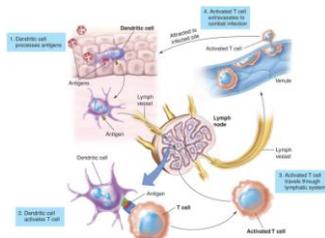
- ▶ When cells have antigen presented on it T cell receptors bind and activate the T-cells
- ▶ T_C Destroy cells with a MHC I antigen complex
- ▶ T_H Bind to Cells with MHC II antigen complexes
 - ▶ Don't kill cell but release cytokines that activate other immune cells
 - ▶ Phagocytes/B-cells/Tc



15-54

Dendritic Cells

- ▶ MHC-antigen complex is necessary to activate T-cells
- ▶ To increase chance of interacting with correct T-cells, dendritic cells migrate to secondary lymphoid organs
 - ▶ Secrete cytokines to attract T-cells
- ▶ Recall macrophages are antigen presenting cells and present on a MHCII platform



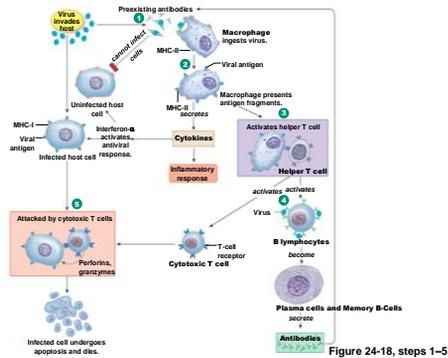
15-49

T Cell Response to a Virus

- ▶ When virus infects body it is phagocytized by macrophage or dendritic cell (antigen presenting cells)
 - ▶ Antigen is presented on MHC II platform
 - ▶ Helper T-cells bind and are activated
 - ▶ Stimulate antibody production
 - ▶ Cytotoxic T cell activity

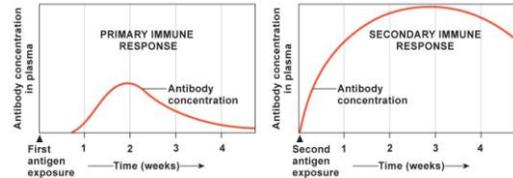
15-56

Immune Response to Viruses



B lymphocytes: Humoral Immunity

► Memory effect in a humoral response



Active Immunity

- Development of a secondary response provides active immunity
- **Immunizations** induce primary responses by inoculating people with pathogens (virulence has been attenuated or destroyed) (vaccinations)
 - Initiate development of B-cell clones that can provide secondary response

15-68

Passive Immunity

- Is immune protection produced by transfer of antibodies to a recipient from a donor
 - Donor was actively immunized
 - Person who receives these ready-made antibodies is passively immunized
 - Used to treat snakebites, rabies, tetanus, hepatitis
 - Natural Passive Immunity!
 - Antibodies from madre passed to fetus during pregnancy
 - During 1st 2-3 days of nursing, mother produces colostrum which is rich in her antibodies

15-72

Allergy (Hypersensitivity)

- Is an abnormal immune response to allergens
- immediate and delayed hypersensitivity
 - Immediate is due to abnormal B-cell response to allergen (antigen); causes effects in secs to mins
 - Caused by foods, bee stings, pollen
 - Delayed is abnormal T-cell response that causes symptoms 24-72 hrs after exposure

15-92

Immediate Allergic Responses

1st exposure dendritic cells stimulate T_H-cells to release cytokines that stimulate b-cells /plasma cells to secrete antibodies that attach to Mast cells and basophils

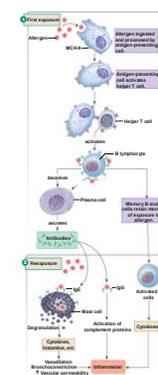
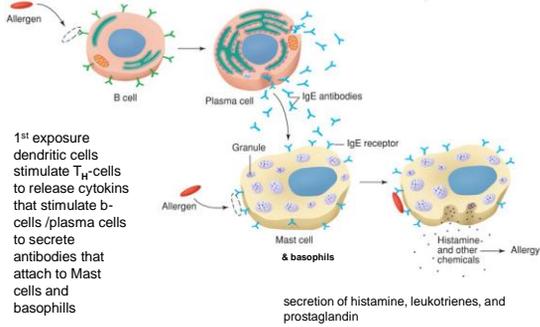


Figure 24-19 (2 of 2)

Immediate Hypersensitivity



15-94

Delayed Hypersensitivity

- ▶ Symptoms take longer to develop (hrs to days)
 - ▶ Is a cell-mediated T-cell response
- ▶ Symptoms caused by secretion of Cytokines, not histamine (i.e., antihistamines don't help)
- ▶ Examples include contact dermatitis caused by poison ivy, oak, or sumac

15-95