Chapter 15 Outline

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

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

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 Aquired (specific) immune system can

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

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

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
### 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

### 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)

### Complement Proteins
- Plasma proteins (globulins)
- Activated by bacteria/virus/pathogen OR Antibodies
  - Inflammation: 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

### 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

### 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 complement proteins (attracts more macrophages)

### 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
Fixation of Complement Proteins

Adaptive (Specific or Acquired) Immunity

- Acquired ability to defend against specific a pathogen by prior exposure to the pathogen
- Humoral 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: Humoral 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 (immunocompetent)
- 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,

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

Antibody Structure

Functions of Antibodies
B Lymphocytes (B cells)
- When B cells bind 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

T-cells (Helper T-cells & Cytotoxic T-cells)
- T-cells attack cells that have a pathogen inside it!
- Killer (Cytotoxic) T Cells
  - Destroy body cells that possess foreign antigens
    1. Virus/fungus
    2. Cancerous cells
  - Kill by cell-mediated destruction
    1. Must be in contact with victim cell to kill it
    2. Secret perforins - create a pore in victim’s membrane and cause lysis
    3. Secrete granzymes which enter cell activate capsases (cause apoptosis)

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
    1. Engulf antigens, partially digest them, and display a piece of the antigen on their surface for T cells to "see"
    2. 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

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
  1. Don’t kill cell but release cytokines that activate other immune cells
  2. Phagocytes/B-cells/Tc

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
  1. Secrete cytokines to attract T-cells
- Recall macrophages are antigen presenting cells and present on a MHCII platform

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
  1. Helper T-cells bind and are activated
    1. Stimulate antibody production
    2. Cytotoxic T cell activity
Immune Response to Viruses

- Macrophage presents antigen fragments.
- Activates helper T cell
- Macrophage ingests virus.
- Infected cell undergoes apoptosis and dies.
- Perforins, granzymes
- MHC II
- MHC I
- Uninfected host cell
- Infected host cell
- Cytotoxic T cell
- T-cell receptor
- Viral antigen
- Attacked by cytotoxic T cells
- Preexisting antibodies
- MHC II
- Interferon-α
- Activates antiviral response.
- Inflammatory response secretes cytokines
- Activates
- Becomes
- Become
- B lymphocytes
- Secrete
- Plasma cells and Memory B cells
- Memory effect in a humoral response
- Antibodies
- Uptake
- Viral antigen
- Helper T cell
- Virus
- Antibodies
- Cytokines
- Immune Response to Viruses
- Cells
- 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

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

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

Immediate Allergic Responses

- 1st exposure dendritic cells stimulate Tc cells to release cytokins that stimulate b-cells/plasma cells to secrete antibodies that attach to Mast cells and basophils
Immediate Hypersensitivity

1st exposure dendritic cells stimulate T cells to release cytokins that stimulate b-cells/plasma cells to secrete antibodies that attach to Mast cells and basophills

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