Resistance and Immunity

Introduction
- Pathogens
  - Disease causing organisms
- Resistance
  - The ability to fight or prevent disease

Disease Causing Organisms
- Bacteria
  - Most common pathogens
  - Anthrax

Disease Causing Organisms
- Bacterial diseases
  - Tuberculosis
  - Cholera
  - Bubonic Plague
  - Tetanus

Effects generally due to toxins or enzymes produced by bacteria

Disease Causing Organisms
- Endotoxins – components of the bacterial cell wall
  - Lipopolysaccharide complex (LPS)
  - Examples: Escherichia coli, Salmonella, Bordetella pertussis

Disease Causing Organisms
- Exotoxins – proteins secreted by bacteria
  - Example: Botulism
    - Clostridium botulinum
    - Toxin prevents acetylcholine release
    - Currently the most toxic substance known
Disease Causing Organisms

- **Antibiotics**
  - May inhibit cell wall formation or protein synthesis in bacteria
  - Overuse may result in resistance
    - MRSA
    - Tuberculosis
      - Both multidrug resistant (MDR-TB) and extensively drug-resistant (XDR TB) exist

- **MRSA**
- **Tuberculosis**
  - Both multidrug resistant (MDR-TB) and extensively drug-resistant (XDR TB) exist

Disease Causing Organisms

- **Viruses**
  - Invade host cells
    - Insert DNA or RNA
      - Control cell's metabolism and produce more viruses
      - Cell death can result from rupture, toxins, depleted essential components
    - Specific to certain types of cells
    - Simple structure
      - Nucleic acids surrounded by a protein coat
      - Not a cell (and therefore not technically alive)

- **Hepatitis (A, B, C, D and E)**
- **Human Immunodeficiency Virus**
  - AIDS
- **Polio**
- **Small pox**
- **Herpes zoster**
  - Chicken pox
  - Shingles

Immune System

- Resistance to disease
- Two intrinsic systems
  - Innate (non-specific) defense system
  - Adaptive (specific) defense system
Immune System

• Innate response
  – Variety of non-specific barriers and mechanisms
  • Body surfaces
  • Phagocytes
  • Natural killer cells (NK)
  • Inflammation
  • Complement system
  • Interferon
  • Fever

**Figure 21.2b**

(b) Events of phagocytosis.

1. Phagocyte adheres to pathogens or debris.
2. Phagocyte forms pseudopods that eventually engulf the particles forming a phagosome.
3. Acidic vesicles react with the phagocytic vesicle, forming a phagolysosome.
4. Hydrolytic enzymes digest the particles, leaving a residual body.
5. Exocytosis of the vesicle removes indigestible and residual material.

Immune System

• Innate response
  – Body surfaces and surface barriers
  • Physical barrier to most microorganisms
  • Components
    – Skin and mucous membranes
    – Oil and sweat
    – Tears
    – Gastric juices
    – Mucus coated hairs in the nose
    – Cilia of upper respiratory tract

Immune System

• Innate Response
  – Phagocytes
  • Functions
    – Engulf particulate matter by endocytosis → phagosome → fuses with lysosome
    – Recognition of foreign material aided by complement or antibody binding
    – Macrophages are the chief phagocytic cells

Immune System

• Innate response
  – Natural killer cells
  • Poorly understood
  • Large granular lymphocytes
  • Target viral infected and tumor cells

Immune System

• Innate response
  – Inflammation
    • Triggered whenever body tissues are injured or infected
    • Three components
      – Prevents the spread of damaging agents
      – Disposes of cell debris and pathogens
      – Sets the stage for repair
Immune System

• Innate response
  – Inflammation
    1. Inflammatory mediators
       – Histamine, kinins, prostaglandins, complement, lymphokines
         • Increased permeability and vasodilation
         • Edema
    2. Chemotaxis
       – Lymphokines → WBC attraction
    3. Removal of pathogens and debris
       – Pus, abscess, granuloma

Chapter 21.4

Immune System

• Innate response
  – Complement system
    • Plasma proteins which stimulate phagocytosis and are cytotoxic
      – Function
        1. Active molecules become embedded in bacteria wall → expand
        2. Potentiates inflammatory response
          – Activation
          1. Antibody binding exposes complement sites
          2. CHO on bacteria bind to complement

Cell Membrane

Immune System

• Innate response
  – Interferon
    • Production stimulated by viral infection
      – Promotes protein synthesis in healthy cells
      – Prevents viral proteins from being formed
      – Activates macrophages and NK cells
      – Target infected cells, possibly malignant cells
    • Used to treat certain chronic viral infections (hepatitis B and C) and certain cancers
**Immune System**

- **Innate response**
  - **Functions**
    - Inhibits bacterial reproduction
    - Improves lymphocyte activity
  - **Activation**
    - Endogenous pyrogens
      - Production related to prostaglandins, also stimulate pain receptors
      - Aspirin interferes with prostaglandin formation

- **The Adaptive Immune Response**
  - **Cells**
    - Antigen-presenting cells (APCs)
      - Dendritic cells, macrophages, B cells
    - Lymphocytes
      - B lymphocytes
      - Produce antibody 
        - Humoral immunity
      - T lymphocytes
      - Cell mediated immunity
      - \( T_{h} , T_{c} , T_{s} \)

- **The Adaptive Immune Response**
  - **Antigens**
    - Surface proteins which initiate a response
    - Self antigens
      - Example: MHC I displaying endogenous self proteins
    - Elicit immune response in other individuals
    - Foreign antigens
      - Example: Infectious agents

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**Immune System**

- The Adaptive Immune Response
  - Components
    - Antibodies and lymphocytes
    - Complement system
    - Phagocytes
  - Specific defense
    - Takes longer to react than the innate system
    - Most effective following a previous exposure

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**Immune System**

- The Adaptive Immune Response
  - Cells
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      - Dendritic cells, macrophages, B cells
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      - B lymphocytes
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        - Humoral immunity
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      - Cell mediated immunity
      - \( T_{h} , T_{c} , T_{s} \)
Immune System

**The Adaptive Immune Response**
- Immunocompetence
  - Ability to recognize specific antigens and bind
  - Occurs in thymus (T-cells) & bone marrow (B-cells)
  - Question: what would happen without the blood-thymus barrier?
- Receptor recognition is specific and genetically determined

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**Antibodies**
- Specialized protein which binds to antigen
- 5 classes: Immunoglobulins
- Structure
  - Constant region
  - Idential in all Ab's in a class
  - Variable region
  - Differ for each Ab

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**Antibody Structure**
- Constant region
- Identical in all Ab's in a class
- Variable region
- Differ for each Ab

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**Antibody Functions**
- Bind antigens = prevent entry into cells
- Bind antigens = alter toxin shape
- Stimulate phagocytosis
- Enhance basic inflammatory response
- Activate complement system

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**Antigenic Determinants**
- Antibodies
  - Neutralization
    - Neutralize part-bound antigens
  - Agglutination
    - Agglutinate path-bound antigens
  - Precipitation
    - Precipitate soluble antigens
  - Complement
    - Complement fixation
  - Stimulate phagocytosis
  - Enhance basic inflammatory response
  - Activate complement system

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**Adaptive Defenses**
- Humoral immunity
  - Antibody
  - Antigen-antibody complex
  - Leads to
    - Cell lysis
    - Agglutination (cell-bound antigens)
    - Precipitation (soluble antigens)
    - Neutralization (masks dangerous parts of bacterial exotoxins; viruses)
  - Plasm and antibodies
    - Fix and activate
    - Enhance
      - Inflammation
      - Chemotaxis
      - Histamine release
      - Complement

Immune System

• The Adaptive Immune Response
  – Foreign antigens and antigen presentation
    • APCs internalize antigen
      – Macrophages = phagocytosis
      – B-cells = receptor mediated endocytosis
      – Dendritic cells = pinocytosis
    • Lysosomal enzymes degrade antigen
    • Small protein segments are displayed on MHC proteins on the APC surface
    – T cells are activated when they contact the APC displaying the specific antigen
      – Secrete interleukins
        » Activates B and T cells specific for that antigen

Physical defenses Humoral immunity

Figure 21.11

Primary response (initial encounter with antigen)

Antigen binding to a receptor on a specific B lymphocyte (B lymphocytes with non-complementary receptors remain inactive)

Proliferation to form a clone

Activated B cells

Plasma cells (effector B cells)

Secreted antibody molecules

Memory B cell—primed to respond to same antigen

Clone of cells identical to ancestral cells

Subsequent challenge by same antigen results in more rapid response

Secondary response (can be years later)

Memory B cells

Plasma cells

Secreted antibody molecules

Adaptive defenses Humoral immunity

Figure 21.12

Primary immune response to antigen A occurs after a delay.

Secondary immune response to antigen A is faster and larger; primary immune response to antigen B is similar to that for antigen A.

Immune System

• Acquired immunity
  – Immunity (antibody production) must be acquired.
    • Exception? (Think back to last term...)
  – Two types
    • Active immunity
    • Passive immunity

Immune System

• Acquired immunity
  – Active Immunity
    • Disease resistance from antigen induced activation
    • 2 sources
      – Infection
      – Vaccination
Immune System

- Acquired immunity
  - Active Immunity
    - Vaccines
      - Killed
        - Influenza, rabies, Salk polio
      - Attenuated (weakened)
        - Smallpox, Sabin polio
      - Toxoid
        - Tetanus, diphtheria
      - Subunit
        - Hepatitis B

- Passively acquired
  - Antibodies transferred into an individual from other sources → immediate protection
  - Artificially acquired
    - Snake venom antiserum
  - Naturally acquired
    - Antibodies cross placenta
    - Breastmilk

Figure 21.13

Immune System

- Disorders
  - Allergy
    - Hypersensitivity to non-pathogenic antigens (allergens)
      - Drugs, insect bites, dander, pollen, dust
    - Stimulate IgE antibody production → bind to cells → stimulate histamine production → bronchiolar constriction, edema, runny nose, watery eyes
  - Anaphylactic shock
    - Severe systemic response
      - Bronchial spasm and hypotension
      - May be fatal
      - Mediated by what leukocytes?

Figure 21.22

Humoral immunity

Naturally acquired infection; contact with pathogen
Artificially acquired vaccine; dead or attenuated pathogens
Naturally acquired Antibodies pass from mother to fetus via placenta; or to infant in her milk
Artificially acquired injection of immune serum (gamma globulin)

Sensitization stage

1. Antigen (allergen) invades body.
2. Plasma cells produce large amounts of class IgE antibodies against allergen.
3. IgE antibodies attach to mast cells in body tissues (and to circulating basophils).
4. Mast cell with fixed IgE antibodies
5. Granules containing histamine

Subsequent (secondary) responses

1. Antigen enters body
2. Antigen combining with IgE attached to mast cell, which triggers degranulation and release of histamine (and other chemicals)
3. Histamine causes blood vessels to dilate and become leaky, which produces edema; stimulates secretion of large amounts of mucus; and causes smooth muscle to contract. (If respiratory system is site of antigen entry, asthma may ensue.)
4. Mast cells release chemicals other than histamine, which combine with IgE antibodies
5. Mast cells release chemicals other than histamine
6. Outpouring of fluid from capillaries
7. Release of mucus
8. Constriction of bronchioles (bronchospasm)
Immune System

• Disorders
  – Autoimmune disease
  • Attack host cells
  • Causes
    – Deficient suppressor T cells
    – Antibody cross reaction
    – Antigenic mutations
  • Examples
    – Lupus
    – Multiple sclerosis
    – Type 1 diabetes
    – Hashimoto's thyroiditis

Transplant Rejection

• Transplants seen as non-self
  – Minimize this by cross matching
  – Artificial replacement parts
  – Use immune suppressing drugs
    • Not always effective
    • Risk of infection

Autoinflammatory Diseases

• Inappropriate activation of innate immunity
• Genetic
• Periodic flares, often with unknown triggers
• Symptoms vary, but usually include...
  – High fever
  – Severe pain
  – Swelling
  – Rash
  – Headaches

Autoinflammatory Diseases

• Examples
  – Familial Mediterranean Fever (FMF)
  – Familial Cold Urticaria (FCU)
  – Muckle-Wells Syndrome (MWOS)
  – Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
  – Pyogenic Arthritis-Pyoderma Gangrenosum-Acne Syndrome (PAPA Syndrome)
  – Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS)
  – Hyper-IgD Syndrome (HIDS)