Microbe-Human Interactions: Infection, Disease and Resistance

Looking Ahead

On completing this chapter, you should be able to:

- Appreciate some concepts relating to infectious disease, including the difference between infection and disease, the stages in the progress of disease, and the methods for transmitting disease;
- Understand the relationships between microbes and their human hosts and list some important factors that contribute to the establishment of infectious disease;
- Summarize some key aspects of nonspecific resistance, including chemical barriers to infection, phagocytosis, and fever;
- Explain how antigens initiate the immune process;
- On completing this chapter, you should be able to:
  - Identify the parts of the immune system and recognize how the process of cell-mediated immunity works;
  - Describe the mechanism by which antibody-mediated immunity yields specific resistance, focusing on the activities of antibodies and the forms of immunity they engender;
  - Understand processes such as allergy and anaphylaxis through which the immune system can have deleterious effects on the human body.

Infection - a condition in which pathogenic microbes penetrate host defenses, enter tissues & multiply

Disease – any deviation from health, disruption of a tissue or organ caused by microbes or their products

Resident flora
- Includes bacteria, fungi, protozoa, viruses and arthropods
- Most areas of the body in contact with the outside environment harbor resident microbes; large intestine has the highest numbers of bacteria
- Internal organs & tissues & fluids are microbe-free
- Bacterial flora benefit host by preventing overgrowth of harmful microbes
- Landscape of the skin
- Distribution of flora
- Colonized regions of the respiratory tract

True pathogens – capable of causing disease in healthy persons with normal immune defenses
- Influenza virus, plague bacillus, malarial protozoan

Opportunistic pathogens – cause disease when the host’s defenses are compromised or when they grow in part of the body that is not natural to them
- Pseudomonas sp & Candida albicans

Overview of infection

Portals of entry
- Skin
- Gastrointestinal tract
- Respiratory tract
- Urogenital tract

Portals of exit
- Respiratory, saliva
- Skin scales
- Fecal exit
- Urogenital tract
- Removal of blood

Infectious dose (ID)
- Minimum number of microbes required for infection to proceed
- Microbes with small IDs have greater virulence
  - 1 rickettsial cell in Q fever
  - 10 bacteria in TB, giardiasis
  - $10^9$ bacteria in cholera

Lack of ID will not result in infection
- Factors affecting I.D. Mechanisms of adhesion/invasion
  - Fimbrae: Allow attachment
  - Flagella: Allow the organism to move
  - adhesive slimes or capsules
  - cilia
  - suckers
  - hooks
  - barbs
  - Mechanisms of adhesion
- Factors affecting I.D. Virulence factors
  - what does the organism use to invade the body
    - exoenzymes – digest epithelial tissues & permit invasion of pathogens
    - Toxigenicity – capacity to produce toxins at the site of multiplication
    - endotoxins – lipid A of LPS of gram-negative bacteria
    - exotoxins – proteins secreted by gram-positive and gram-negative bacteria
    - antiphagocytic factors – help them to kill or avoid phagocytes, include leukocidins and capsules
- Patterns of infection
  - localized infection – microbes enter body & remains confined to a specific tissue
  - systemic infection – infection spreads to several sites and tissue fluids usually in the bloodstream
  - focal infection – when infectious agent breaks loose from a local infection and is carried to other tissues
  - Patterns of infection
  - Mixed infection – several microbes grow simultaneously at the infection site
  - Primary infection – initial infection
  - Secondary infection – another infection by a different microbe
- Diagnosis
  - Sign – objective evidence of disease as noted by an observer
  - Symptom – subjective evidence of disease as sensed by the patient
  - Sequelae – long-term or permanent damage to tissues or organs
- Epidemiology
  - The study of the frequency and distribution of disease & health-related factors in human populations
  - Surveillance – collecting, analyzing, & reporting data on rates of occurrence, mortality, morbidity and transmission of infections
  - Reportable, notifiable diseases must be reported to authorities
  - Centers for Disease Control and Prevention
    - (CDC) in Atlanta, GA – principal government agency responsible for keeping track of infectious diseases nationwide
  - Prevalence – total number of existing cases with respect to the entire population usually represented by a percentage of the population
  - Incidence – measures the number of new cases over a certain time period, as compared with the general healthy population
  - Mortality rate – the total number of deaths in a population due to a certain disease
  - Morbidity rate – number of people afflicted with a certain disease
- Endemic – disease that exhibits a relatively steady frequency over a long period of time in a particular geographic locale
- Sporadic – when occasional cases are reported at irregular intervals
- Epidemic – when prevalence of a disease is increasing beyond what is expected
- Pandemic – epidemic across continents
- Patterns of disease occurrence
- Reservoirs of infection
  - Primary habitat in the natural world from which a pathogen originates
  - Living reservoirs may or may not have symptoms
  - Asymptomatic carriers
  - Passive carriers
  - **Vectors** – live animal that transmits infectious disease
  - Nonliving reservoirs – soil, water
- Types of carriers
- Vectors
- Patterns of transmission
  - Direct contact
    - Kissing, sharing body fluids,
  - Indirect contact
    - Vehicle – inanimate material, food, water, biological products, **fomites**
    - Airborne – droplet nuclei, aerosols
- Nosocomial infections
  - Diseases that are acquired during a hospital stay
  - Most commonly involve urinary tract, respiratory tract, & surgical incisions
  - Most common organisms involved gram-negative intestinal flora, *E. coli*, *Pseudomonas*, *Staphylococcus*
- Nosocomial infections
- Immunity
  - Resistance is the ability to ward off disease
  - lack of resistance is termed susceptibility
- Nonspecific resistance to disease
  - general defensive mechanisms effective on a wide range of pathogens (disease producing microbes)
- Specific resistance or immunity is ability to fight a specific pathogen
  - cell-mediated immunity
  - antibody-mediated immunity
- Nonspecific Resistance to Disease
  - Immediate protection against wide variety of pathogens & foreign substances
  - lacks specific responses to specific invaders
  - Mechanisms function regardless of type of invader
  - external mechanical & chemical barriers
  - internal nonspecific defenses
    - antimicrobial proteins
    - natural killer cells & phagocytes
    - inflammation & fever
    - Skin & Mucous Membranes
  - **Mechanical protection**
    - skin (epidermis) closely packed, keratinized cells
    - shedding helps remove microbes
    - mucous membrane secretes viscous mucous
    - cilia & mucus trap & move microbes toward throat
    - washing action of tears, urine and saliva
  - **Chemical protection**
    - sebum inhibits growth bacteria & fungus
    - perspiration lysozymes breakdown bacterial cells
    - acidic pH of gastric juice and vaginal secretions destroys bacteria
  - **Internal Defenses**
    - Antimicrobial proteins discourage microbial growth
    - interferons
      - produced by virally infected lymphocytes & macrophages
- diffuse to neighboring cells to induce synthesis of antiviral proteins
  - complement proteins
    - inactive proteins in blood plasma
    - when activated enhance immune, allergic & inflammatory reactions
  - transferrins
    - iron-binding proteins inhibit bacterial growth by reducing available iron
- Stages of Inflammation
  - Vasodilation & increased permeability of vessels
  - caused by histamine from mast cells, kinins from precursors in the blood, prostaglandins from damaged cells, and leukotrienes from basophils & mast cells
  - occurs within minutes producing heat, redness & edema
  - pain can result from injury, pressure from edema or irritation by toxic chemicals from organisms
  - blood-clotting factors leak into tissues trapping microbes
  - Phagocyte emigration
    - within an hour, neutrophils and then monocytes arrive and leave blood stream (emigration)
- Tissue repair
- Fever
  - Abnormally high body temperature that occurs because the hypothalamic thermostat is reset
  - Occurs during infection & inflammation
  - bacterial toxins trigger release of fever-causing cytokines such as interleukin-1
  - Benefits
    - intensifies effects of interferons, inhibits bacterial growth, speeds up tissue repair
- Lymphatic Organs & Tissues
  - Widely distributed throughout the body
  - Primary lymphatic organs
    - provide environment for stem cells to divide & mature into B and T lymphocytes
    - red bone marrow gives rise to mature B cells
    - thymus is site where pre-T cells from red marrow mature
  - Secondary lymphatic organs & tissues
    - site where most immune responses occur
    - lymph nodes, spleen & lymphatic nodules
- Natural Killer Cells & Phagocytes
  - NK cells kill a variety of microbes & tumor cells
    - found in blood, spleen, lymph nodes & red marrow
    - attack cells displaying abnormal MHC antigens
  - Phagocytes (neutrophils & macrophages)
    - ingest microbes or particulate matter
    - macrophages developed from monocytes
    - fixed macrophages stand guard in specific tissues
    - histiocytes in the skin, kupffer cells in the liver, alveolar macrophages in the lungs, microglia in the brain & macrophages in spleen, red marrow & lymph nodes
    - wandering macrophages in most tissue
- Phagocytosis
- Chemotaxis
  - attraction to chemicals from damaged tissues, complement proteins, or microbial products
  - Adherence
  - attachment to plasma membrane of phagocyte
  - Ingestion
    - engulf by pseudopods to form phagosome
- Digestion & killing
- merge with lysosome containing digestive enzymes & form lethal oxidants
- exocytosis residual body

- Specific Resistance: Immunity
  - Immunity is body's ability to defend itself against specific foreign material or organisms
    - bacteria, toxins, viruses, cat dander, etc.
    - Diffs from nonspecific defense mechanisms
    - specificity----recognize self & non-self
    - memory----2nd encounter produces even more vigorous response
    - Immune system is cells and tissues that produce the immune response
    - Immunology is the study of those responses
  - Antigens
    - Molecules or bits of foreign material
      - entire microbes, parts of microbes, bacterial toxins, pollen, transplanted organs, incompatible blood cells
    - Get past the body's nonspecific defenses
    - enter the bloodstream to be deposited in spleen
    - penetrate the skin & end up in lymph nodes
    - penetrate mucous membrane & lodge in associated lymphoid tissue

- Major Histocompatibility Complex Antigens
  - All our cells have unique surface markers (1000s molecules)

- Function
  - if cell is infected with virus MHC contain bits of virus mark cell so T cells recognize a problem
  - if antigen-presenting cells (macrophages or B cells) ingest foreign proteins, they will display components part of their MHC

- Histocompatibility Testing
  - Histocompatibility is a similarity of MHC antigens on body cells of different individuals
  - tissue typing must be done before any organ transplant
  - can help identify biological parents

- Types of Mature T Cells
  - Helper T cells
  - Cytotoxic (killer) T cells
  - Memory T cells
  - Helper T Cells
    - Display a marker called CD4 on surface. Also known as T4 cells or TH cells
      - Recognize antigen fragments associated with MHC
  - Cytotoxic T Cells
    - Display CD8 on surface
    - Known as T8 or Tc or killer T cells
    - cells infected with virus
    - tumor cells
    - tissue transplants
  - Memory T Cells
    - T cells from a clone that did not turn into cytotoxic T cells during a cell-mediated response
    - Available for swift response if a 2nd exposure should occur

- Immunological Surveillance
  - Cancerous cell displays weird surface antigens (tumor antigens)
  - Surveillance = immune system finds, recognizes & destroys cells with tumor antigens
    - done by cytotoxic T cells, macrophages & natural killer cells
- most effective in finding tumors caused by viruses
- Transplant patients taking immunosuppressive drugs suffer most from viral-induced cancers

- Antibody-Mediated Immunity
  - Millions of different B cells that can recognize different antigens and respond
  - B cells sit still and let antigens be brought to them
  - stay put in lymph nodes, spleen or peyer’s patches
  - Once activated, differentiate into plasma cells that secrete antibodies
  - Antibodies circulate in lymph and blood
  - combines with epitope on antigen similarly to key fits a specific lock

- Antibody Structure
  - Glycoproteins called immunoglobulins
  - 4 polypeptide chains
  - hinged midregion lets assume T or Y shape
  - tips are variable regions -- rest is constant region
  - 5 different classes based on constant region
    - IgG, IgA, IgM, IgD and IgE
  - tips form antigen binding sites

- Immunological Memory
  - Primary immune response
    - first exposure to antigen
      - response is steady, slow
      - memory cells may remain for decades
  - Secondary immune response with 2nd exposure
    - 1000’s of memory cells proliferate & differentiate into plasma cells & cytotoxic T cells
    - antibody titer is measure of memory (amount serum antibody)
    - recognition & removal occurs so quickly not even sick

- Self-Recognition & Immunological Tolerance
  - T cells must learn to recognize self (its own MHC molecules) & lack reactivity to own proteins
  - self-recognition & immunological tolerance

- T cells mature in thymus
  - those can’t recognize self or react to it
  - only 1 in 100 emerges immunocompetent T cell

- B cells develop in bone marrow same way

- Aging
  - More susceptible to all types of infections and malignancies
  - Response to vaccines is decreased
  - Produce more autoantibodies
  - Reduced immune system function
  - T cells less responsive to antigens
  - age-related atrophy of thymus
  - decreased production of thymic hormones
  - B cells less responsive
  - production of antibodies is slowed

- Destructive immunity

- Hemolytic disease of the newborn
  - Allergic reactions
  - Anaphylactic shock
- Hay fever
- Hypersensitivities
- Autoimmune diseases
  - Systemic Lupus
  - Rheumatoid arthritis
  - Sjogrens Syndrome
  - Multiple Sclerosis