Chapter 4
Infectious Health Problems

Overview of Today’s Lecture

• Factors in Infection
• Overview of the classes of microorganisms
• Infection and Injury
  – Classes of Microorganisms
    • Bacteria
    • Viruses
    • Rickettsiae, Mycoplasma, Chlamydia
    • Fungi
    • Parasites
  – Communicable Disease
  – Clinical Manifestations
  – Antimicrobial Therapy
• Immunodeficiency

Review: Innate Antimicrobial Protection

Introduction to Infectious Disease

- **Infectious disease**
  - Transmissible (infectious) agent (microbes)
  - Invades through physical barriers (innate defenses)
  - Overcomes innate and adaptive immune defenses of host
  - Causes injury and disease (now called a *pathogen*).

- **Endemic rate** – normal expected rate of infection

- **Epidemic** – greater than normal infection rate

- **Commensal relationship** – organism benefits, we are not harmed

- **Parasites** – organisms that need the host to survive

Microorganism and Human Relationship

- **Mutual relationship**
  - Normal flora
  - Relationship can be breached by injury
    - Leave their normal sites and cause infection elsewhere

- **Opportunistic microorganisms**
  - Normally held in check by immune system/defenses
  - Do not usually cause disease except when a person’s decreased immunity/defenses allow it

Classes of Microorganisms

- Classes of Microorganisms (approx. from smallest to largest)
  - **Prions** (misfolded proteins, PrP)
  - **Viruses**
  - **Chlamydia** (pathogenic bacteria, especially common in STIs)
  - **Rickettsia** (non-motile, gram negative bacteria)
  - **Mycoplasma** (bacterial genus lacking a cell wall)
  - **Bacteria**
  - **Fungi**
  - **Protozoa** (unicellular, eukaryotic, usually motile organisms)
  - **Helminths** (multicellular, parasitic worms)
  - **Ectoparasites** (multicellular, insect-like, invade skin)
Factors Influencing Pathogen’s Infectivity

- True pathogens can circumvent the body’s normal defenses, depending on the following factors:
  - Pathogenicity
    - Ability of an agent to produce disease
    - Success depends on communicability, infectivity, extent of tissue damage, and virulence
  - Immunogenicity
    - Ability of pathogens to induce an immune response
  - Infectivity
    - Ability of pathogens to invade and multiply in the host
      - Involves attachment to cell surface, release of enzymes, escape from phagocytes, spread through lymph and blood to tissues
  - Virulence
    - Capacity of a pathogen to cause severe disease; for example, measles virus is of low virulence, while rabies virus is highly virulent

Factors Influencing Infection (cont’d)

- Communicability
  - Ability to spread from one individual to others and cause disease; measles & pertussis spread very easily, HIV is of lower communicability
- Mechanism of action
  - How the microorganism damages tissue
- Portal of entry
  - Route by which a pathogenic microorganism infects the host
    - Direct contact
    - Inhalation
    - Ingestion
    - Bites of an animal or insect
- Toxigenicity
  - Ability to produce soluble toxins or endotoxins, factors that greatly influence the pathogen’s degree of virulence
- Tropism – Preference for infect a particular tissue or cell

Communicable Disease

- Communicable Diseases are those spread from person to person
  - Usually by infected blood, body fluids
  - All communicable diseases are infectious
- Modes of Transmission (Mn: DIVIDE)
  - Direct Contact
  - Ingestion
  - Vectors
  - Indirect Contact
  - Droplets (airborne)

Host Reaction to Infectious Organisms

- **Viruses**
  - Chronic inflammation
  - Lymphocytes and monocytes
  - Can be cytopathic or cytoproliferative

- **Bacteria**
  - Suppurative (purulent) inflammation – acute
  - Neutrophil infiltrate at site and in blood (neutrophilia)
  - Exceptions: Chlamydia and Treponema pallidum (syphilis)
  - Exceptions: Mycobacterium tuberculosis -> granulomatous (chronic) inflammation with lymphocytes and monocytes forming nodules

- **Fungi**
  - Granulomatous inflammation

- **Parasitic worms (helminths)** – eosinophils

- **Protozoa** – Variable

The Natural Course of Infection

Examples of Pathogen Defense Mechanisms

- **Bacteria**
  - Produce surface coats that inhibit phagocytosis
    - Outer coat: gram+ org, waxy coat, LPS
  - Produce toxins (leukocidins) that destroy neutrophils
  - Molecules that destroy Ig’s: IgA proteases

- **Viruses**
  - Many can mutate within cells where they are not available to immune and inflammatory mechanisms
  - Not available to antibodies in circulation
  - Antigenic variations:
    - Antigenic drift – mutation in key surface antigens
    - Antigenic shifts – genetic recombination that changes antigenic properties
Viral Infections

- Characteristics of viruses:
  - Dependent on host cells for their replication
  - No metabolism
  - Simple organism
    - Genetic material
    - Surrounding layer of proteins (capsid)
  - Usually a self-limiting infection
  - Spreads cell to cell
  - Virus then uncoats in cytoplasm
  - DNA virus replicates in nucleus (except poxviruses)
  - RNA virus replicates in cytoplasm (except influenza/retroviruses)
  - Post-infection immunity depends on whether or not virus mutates regularly

Acute (Transient) Viral Infections

- Respiratory-tropic
  - Rhinoviruses (100 varieties); common cold
    - Usually spread by person-to-person contact
    - Respiratory droplet (airborne) transmission is possible
  - Adenoviruses; Tonsillitis, conjunctivitis, bronchiolitis
  - Respiratory Syncytial Virus (RSV)
    - Major cause of lower respiratory tract infection in children
    - Bronchiolitis, pneumonia
  - Influenza (influenza viruses type A and B)
    - Flu-like symptoms (fever, chills, nasal congestion, cough, myalgia, malaise)
    - Spread mainly by respiratory droplets
    - May cause problems in "at-risk" segments of the population

- Gastrointestinal-tropic (usually fecal contamination)
  - Rotavirus
    - Most common cause of severe diarrhea in infants and young children
    - Fecal-Oral route transmission
    - Vomiting, severe diarrhea, dehydration
    - Common in daycare centers
  - Norovirus (Norwalk virus)
    - 90% of non-bacterial gastroenteritis in older children and adults
    - Caused by fecally contaminated food, water
    - Transmission by person-to-person contact or aerosolization
    - Prevalent in "close" quarters: Cruise ships, long-term care facilities, overnight camps, hospitals, prisons, dormitories
    - Nausea, abdominal pain, vomiting, watery diarrhea
Acute (Transient) Viral Infections

- Other transient viral infections
  - Measles (rubeola)
    - Highly contagious; nasal and oral secretions
    - Characteristic maculopapular rash (flat, red area on skin covered with small confluent bumps)
    - Rash-like Koplick spots on check mucosa
  - Mumps
    - Contagious (but less than measles)
    - Tropic for salivary glands, esp. parotid
  - Rubella (German measles)
    - Contagious (but less than measles); droplet
    - May be asymptomatic or brief, mild febrile illness
  - Coxsackie (Types A and B)
    - Type A is tropic for oral mucosa and skin (hand-foot-and-mouth disease); usually infants/children
    - Type B is tropic for heart, lung, pancreas, and nervous system
    - No vaccine
  - Hepatitis A (HAV)
    - Epidemic, fecal-oral transmission

Persistent (Chronic) Viral Infections

- Immune system does not eliminate virus
  - Latent – recurrent flare-ups
  - Productive – chronic inflammation and tissue injury
  - Transformative – transformation of normal tissue into neoplasm
- Latent
  - Herpes simplex virus (HSV)
    - Type 1 (mainly oral cold sores) and type 2 (mainly genital)
    - Small, painful blisters in skin or mucosa
    - Tropic for sensory axons; then travels to neuron cell body
    - No vaccine (acyclovir can limit and lessen symptoms)
  - Herpes zoster (varicella-zoster) virus – related to HSV (above)
    - Acute infection is chickenpox (children typically)
    - Usually mild, short-term constitutional symptoms except in immunocompromised
    - Tropic for neurons, persists, and may reactivate to cause shingles (adults)
  - Cytomegalovirus (variant of herpesvirus)
    - Tropic for blood monocytes; asymptomatic or may mimic infectious mononucleosis
    - Crosses the placenta, be transmitted to newborn through vaginal secretions or milk
    - Most common opportunistic in AIDS patients
- Transformative Virus Infections
  - Epstein-Barr Virus (EBV)
    - Agent of infectious mononucleosis (IM), usually young adults
    - Chronic infection linked to some lymphomas and carcinomas
  - Human Papilloma Virus (HPV)
    - Tropic for skin and squamous mucosa
    - Some asymptomatic, some skin warts, anogenital warts, cervical dysplasia/cancer
    - Vaccine available for most types
Bacteria

- Single-cell
- Single chromosome, no nucleus (prokaryotic)
- Classified by
  - Shape (coccis, bacilli, coccobacilli)
  - Requirement for oxygen
  - Gram stain (positive or negative)
  - Acid fast (mycobacterium, nocardia)


Bacterial Virulence & Toxins

- Bacterial toxin production
  - Exotoxins
    - Proteins and Enzymes released during growth
    - Enzymatically inactivate or modify key cellular components
    - Diphtheria toxin; inhibits cellular protein synthesis
    - Botulinum toxin; decreases release of acetylcholine causing flaccid paralysis
    - Tetanus toxin; decreases release of glycine/GABA causing spastic paralysis
  - Immunogenic
    - Antitoxin production
    - Can produce antibodies against exotoxins
    - Some vaccines available
  - Endotoxins
    - Lipopolysaccharides (LPS) contained in the cell walls of gram-negative organisms released during cell destruction
    - Pyrogenic (fever-producing) effects; endotox/sepptic shock

Bacterial Virulence

- Bacteria in blood
  - Presence = bacteremia
  - Growth = septicemia (sepsis)
    - Failure of immune system to check bacterial growth

- Invasion of blood by bacteria
  - A result of a failure of the body’s defense mechanisms
  - By gram-negative bacteria
  - Endotoxins released in the blood
    - Release of vasoactive peptides and cytokines
    - Produce widespread vasodilation leading to septic (endotoxic) shock

Bacteria - Cocci

- Gram positive cocci
  - Most are aerobic
  - Usually cause acute, intense, pyogenic infections
  - Staphylococci (grow in tight clusters), e.g., S. aureus
  - Streptococci (grow in twisted chains)
    - Identified by
      - Antigenic properties into groups (A, B, D, etc.)
      - Character of hemolysis they cause (green (α), clear (β), none)
    - Examples:
      - Streptococcus pneumoniae (pneumococcus) causes lobar pneumonia
      - Streptococcus pyogenes

- Gram negative cocci
  - Neisseria are only important ones; N. meningitidis
  - Causes life-threatening meningitis, especially in children

Streptococcal Diseases

Figure from: McConnell, The Nature of Disease, 2nd ed., Wolters Kluwer, 2014
Bacteria - Bacilli

- **Gram positive bacilli**
  - Illnesses caused are typically species-specific
  - Examples:
    - Corynebacterium Diptheriae (diptheria)
    - Listeria monocytogenes (food borne infections)
    - Bacillus anthracis (anthrax)
    - Clostridium (C. difficile, C. perfringens, C. tetani, C. botulinum)

- **Gram negative bacilli**
  - Intestinal infections
    - H. pylori, E. coli, Salmonella, Shigella, Vibrio cholera
  - Respiratory infections
    - H. influenza, Legionella pneumophila, Bordatella pertussis, Pseudomonas aeruginosa

Rickettsiae, Mycoplasmas, and Spirochetes

- Have characteristics of both bacteria and viruses

  - **Rickettsiae**
    - Obligate intracellular parasites
    - Also gram-negative bacteria
    - Target human endothelium

  - **Mycoplasmas**
    - Lack cell wall
    - Survive on surface of host cells
    - Commonly found in human urogenital & respiratory tracts

  - **Spirochetes**
    - Gram negative, flagellated, thin, motile, corkscrew shaped
    - Example: Borrelia Burgdorferi (Lyme disease)

Mycobacteria Cause Chronic Infection

- Mycobacteria are aerobic, acid-fast, comma shaped
- M. tuberculosis, M. lepreae (leprosy), M. avium (common in AIDS opportunistic infection), M. bovinum
- **Mycobacterium Tuberculosis**
  - Tuberculous (TB) is a major, chronic, progressive, and communicable disease
  - Lungs most commonly affected; vertebræ & meninges also
  - Distinctive granulomatous inflammation
    - Monocyte and lymphocyte infiltration
    - Caseous necrosis with crumbly, cheese-like necrotic tissue
  - Incidence has declined in US except in certain target populations
    - poor, crowded, debilitated, and aged at risk
    - immunocompromised, DM, chronic lung diseases, malnutrition, alcoholism
Pathogenesis of Tuberculosis

Figure from: McConnell, The Nature of Disease, 2nd ed., Wolters Kluwer, 2014

Pathology of Tuberculosis

• 1st TB
  - Small focus of granulomatous inflammation
  - Scarring causes calcified, necrotic lesions, Ghon tubercles, in lungs (primary infection site)
  - When Ghon tubercles also appear in hilar LN > Ghon complex

• 1st progressive TB (only about 5% of clinical cases)
  - Typically seen in children and target population
  - Bacterial spread is more extensive than primary TB
  - May ‘seed’ other organs through blood (miliary TB)
  - NO caseating granulomas (Why?)

• 2nd TB (reactivation TB; about 95% of clinical cases)
  - Characterized by caseating granulomatous inflammation since this occurs in previously sensitized individuals
  - Fewer granulomas, but they are typically larger
  - Lesions typically seen in apex of lung
  - May cavitate into airways and facilitate spread through coughing

Diagnosis and Treatment of TB

• Typically mild clinical onset with fever, night sweats, mild malaise, weight loss, and poor appetite
  - If neglected, causes wasting (‘consumption’)
  - If progresses, productive cough perhaps with blood

• Test is the Purified Protein Derivative (PPD)
  - Skin test for infection, not disease
  - After 2 weeks post infection, positive test
  - Almost all negative tests have not been infected
  - 48-72 hours after PPD injection (on volar surface of forearm)
    - Must be induration (hard, tense), not just erythematous, to be positive
    - < 5 mm: high risk for development of active TB
    - 5-10 mm: increased risk for development of active TB
    - > 10 mm: unlikely to develop to active TB
Fungal Infection

- Characteristics of fungi
  - Relatively large microorganisms
  - Thick rigid cell walls without peptidoglycans (resist penicillin and cephalosporins)
  - Eukaryotic (nucleated)
  - Exist as
    - single-celled yeasts; facultative anaerobes
    - multi-celled molds; aerobic
  - Sometimes both (dimorphic fungi)
  - Reproduce by simple division or budding

Infection and Injury - Fungal Infection

- Pathogenicity
  - Adapt to host environment
    - Wide temperature variations, digest keratin, low oxygen
    - Suppress the immune defenses
    - Usually controlled by phagocytes, T lymphocytes
  - Diseases caused by fungi are called mycoses
    - Superficial, deep, endemic (dimorphic fungi), or opportunistic
  - Fungi that invade the skin, hair, or nails are known as dermatophytes (superficial mycoses)
    - The diseases they produce are called tineas (ringworm)
      - Tinea capitis, tinea pedis, and tinea cruris
  - Deep fungal infections are life threatening and are commonly opportunistic (e.g., with antibiotics or pH changes).
  - *Changes that alter normal flora promote fungal infections

Infection and Injury - Fungal Infection

- Candida albicans
  - Usually superficial as commensals on skin and mucous membranes
  - Candidiasis or moniliasis
  - Spread from superficial structures more serious
  - Aspergillus is another commensal that can become dangerous in immunocompromised individuals

- Deep mycoses
  - B. dermatidis – Blastomycesis (endemic)
  - Coccidioides – Coccidiomycosis (SW US)
  - Histoplasma – Histoplasmosis (bat guano)
  - Pneumocystis jiroveci only occurs in immunocompromised individuals

Clinical Models – Tinea (Fungus)

- Group of fungal skin diseases that occur in several locations
  - Feet (tinea pedis)
  - Nails (tinea unguium)
  - Scalp (tinea capitis)
  - Groin (tinea cruris)
  - Skin (tinea corporis/ringworm, tinea versicolor)

- Pathophysiology
  - Major route of transmission is by direct contact with infected reservoir
  - Some predisposing factors
    - Exposure to moist conditions
    - Genetic predisposition
    - Immunocompromise
    - Sharing of hygiene facilities with infected individuals
  - Fungus (dermatophyte) attaches to keratinized cells and causes thickening
  - May be complicated by bacterial superinfection or invasive dermatophyte invasion

Infection and Injury - Parasitic Infection

- Parasite – organism that benefits at host’s expense

- Major classes of parasites
  - Unicellular, nucleated, motile protozoa
    - Include malaria, amoebae, flagellates
  - Cases of Primary Amoebic Meningoencephalitis in 2013 caused by Naegleria fowleri
  - Large worms (helminths)
    - Flatworms (flukes), roundworms (nematodes), tapeworms (cestodes)
    - Ectoparasites – life on surface of host: lice, scabies,

Insect vectors; Infect blood

Protozoa

- Malaria (Plasmodium spp.; most common protozoan infection worldwide)
  - Vector is mosquito
  - Invades/destroy RBCs
- Leishmaniasis (Leishmania spp.)
  - Chronic, inflammatory disease
  - Infects WBC, skin, mucous membranes, viscera
  - Vectors are sandflies
- Trypanosomiasis (Trypanosoma spp.)
  - Infects blood
  - Vectors are several types of insects
  - African sleeping sickness; Chagas disease (cats are reservoir)
- Amebiasis (Entamoeba histolytica)
  - Consumption of fecally contaminated food
  - Intestine (diarrhea), portal blood to form amebic abscesses, brain and lung
- Giardiasis (Giardia lamblia; most common protozoan infection in US)
  - Ingesting fecally contaminated water or produce (chlorination not effective)
  - Acute or chronic diarrhea when symptomatic
- Cryptosporidiosis (Cryptosporidium, also called microsporidiosis)
  - In soil, food, water, fecally contaminated surfaces
  - Diarrhea in immunocompromised
### Helminths (worms)

- **Peripheral blood eosinophilia** is a hallmark
- **Roundworms (nematodes)**
  - *Filaria*<br>  Vector in mosquito<br>  - Infects Lymphatics and subcutaneous tissue<br>  - Vector usually of women and aged (elephantiasis)<br>  - **Intestinal roundworms** (Usually tropical areas; oral-fecal contamination; intestine)<br>  - **Ascaris** (Ascaris spp.) – intestinal bleeding/obstruction, anemia (feed on blood),<br>  - **Hookworms** – intestinal bleeding, anemia<br>  - **Parasites** – common pediatric infection in US; intestine, perianal area<br>  - **Trichina** – eating inadequately cooked pork; spread to muscle (pain, fever)<br>  - **Flatworms (flukes, trematodes)**<br>  - Infect blood vessels, GI tract, lungs, or liver<br>  - **Schistosomiasis** – most common of all worm infections; mail vector<br>  - **Tapeworms (cestodes)**<br>    - 3 stages: eggs, larvae, adult<br>    - Internal infection<br>    - Adults are named for their intermediate host, e.g., fish, beef, pork; larvae are in muscle<br>    - When intermediate host is eaten (undercooked), larvae develop<br>    - **Echinococcosis (hydatid disease)**

### Sexually Transmitted Infections (STIs)

- Infections communicated by sexual contact<br>  - Can be caused by any type of microorganism<br>    - *Viruses*, e.g., genital and anorectal warts by HPV, genital herpes, HIV<br>    - *Bacteria*, e.g., syphilis, gonorrhea, Chlamydia, Mycoplasma<br>    - *Parasites*, e.g., trichomoniasis (amebic), scabies (skin mites), lice (pediculosis)<br>  - Some non-STI infections can be transmitted sexually, e.g., viral hepatitis<br>  - Problematic because many cases are asymptomatic and this increases the risk of transmission<br>  - Safe-sex practices can prevent STIs<br>  - Chlamydia (C. trachomatis) is most common STI in the world<br>  - Chlamydia and gonorrhea (N. gonorrhoeae) are the most common causes of STI-related infertility

### Infection and Injury – Countermeasures; Antimicrobials

- **Antimicrobials (antibiotics)**<br>  - Usually products of fungi or bacteria that inhibit growth of bacteria<br>  - **Bactericidal** (kill) vs. **bacteriostatic** (inhibit growth)<br>  - General mechanisms of most antibiotics<br>    - Inhibit synthesis of cell wall and other proteins<br>    - Damage cytoplasmic membrane<br>    - Alter metabolism of nucleic acid, inhibition of DNA synthesis<br>    - Modify energy (folic acid) metabolism<br>  - **Antimicrobial resistance mechanisms**<br>    - Genetic mutations transmitted to other bacteria by plasmid exchange<br>    - Inactivation and/or breakdown of antibiotic<br>    - Multidrug transporters in bacterial cell membrane inhibit uptake<br>    - Multiple antibiotic-resistance bacteria (e.g., MRSA, VISA, VRSA, etc.)<br      - Major problem in hospitals<br      - Inadequate patient compliance with antibiotic regimen<br      - Overuse/over-prescribing of antibiotics by healthcare professionals
Vaccines

- Biologic preparations of weakened or dead pathogens
  - Live, attenuated strains; not enough virus to cause disease (except in immunocompromised individuals)
  - Heat killed virus; outer protein coat stays intact to promote immune response
- Recombinant viral protein
- Long lasting immunity (artificial, active)
  - Primary response is short-lived
  - Booster increases secondary response
- CDCP schedules @ [http://www.cdc.gov/vaccines/schedules/index.html](http://www.cdc.gov/vaccines/schedules/index.html)
- Vaccines against bacterial exotoxins are called ‘toxoids’, e.g., DPT
- Reluctance to vaccinate
  - Most objections are based on incomplete or incorrect information
  - Complications are rare
  - Removal of thimerosal (Hg containing) from most vaccines in 2001 has lessened the risk and increased the favorable perception about vaccines