Introduction to Medical Microbiology
MHD I 2018-19

MHD Microbiology Curriculum

• **Principles of Bacteriology**
  • MHD I Block 2 (August 14-27)
• **Bacteria**
  • MHD I Block 3 (August 28-September 17)
    • Mycobacteria (MHD I Block 5)
    • H. Pylori, Campylobacter, Vibrio (MHD II Block 1)
• **Fungi**
  • MHD I Block 5
• **Parasites**
  • MHD II Block 3
• **Viruses**
  • MHD II Block 5

MHD Microbiology Curriculum

• **Infectious Disease**
  • Common or prototypic infections of organ systems will be discussed
  • During individual lectures throughout MHD
  • Dedicated clinical correlate sessions
    • Cardiac/Endovascular Infections (Cardiac Block)
    • Urinary Tract Infections (Renal Block)
    • Respiratory Tract Infections (Pulmonary Block)
    • CNS Infections (Neuroscience Block)
    • Clinical Aspects of Human Immunodeficiency Virus (Virus Block)
MHD Microbiology Curriculum

- MHD Small Group Sessions
  - Introduction to Bacteriology Block
    - Bacterial Physiology
    - Bacterial Genetics
  - Bacteriology Block
    - 4 small group sessions - all cases focused on bacterial infections
    - Integrate Pharm/Therapeutics - antibiotics and approach to therapy
  - Virology Block
    - 3 Small Group sessions focused on Viral Infections
  - Multiple other small group sessions will also include cases focused on infections, approach to diagnosis and approach to therapy

MHD Microbiology Curriculum

- Sessions dedicated to Self-Assessment and Review
  - Bacteriology - Self-Assessment Quizzes
  - Mycology – Seminar
  - Parasitology – Seminar
  - Virology - Seminars

MHD Microbiology Curriculum

- Educational Resources
  - Texts
    - Murray's Medical Microbiology
    - Robbins
  - Resources for Review of Material
    - Flashcards
    - Charts
    - Animated videos
Questions?

Introduction to Medical Microbiology

Objectives

• Classify common human pathogens within the appropriate Taxonomic Class
• Summarize routes of entry and dissemination of microbes
• Summarize modes of transmission of microbes
• Summarize means by which microbes may evade the host’s immune system
• Describe the spectrum of inflammatory responses to infection and classic examples of microbes that cause each response

Classify Common Human Pathogens Within The Appropriate Taxonomic Class
Categories of Infectious Agents

<table>
<thead>
<tr>
<th>Category</th>
<th>Taxonomic Category</th>
<th>Size</th>
<th>Propagation</th>
<th>Site(s)</th>
<th>Example(s)</th>
<th>Disease(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prions</td>
<td>Intracellular</td>
<td>&lt;20 nm</td>
<td>Prion protein</td>
<td>Prion protein</td>
<td>Prion protein</td>
<td>Creutzfeldt-Jacob disease</td>
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<tr>
<td>Viruses</td>
<td>Obligate intracellular</td>
<td>20–300 nm</td>
<td>Poliovirus</td>
<td>Poliovirus</td>
<td>Poliovirus</td>
<td>Poliomyelitis</td>
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<tr>
<td>Bacteria</td>
<td>Obligate intracellular</td>
<td>0.2–15 µm</td>
<td>Chlamydia trachomatis</td>
<td>Chlamydia trachomatis</td>
<td>Trachoma, urethritis</td>
<td></td>
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<tr>
<td></td>
<td>Facultative intracellular</td>
<td></td>
<td>Streptococcus pneumoniae</td>
<td>Streptococcus pneumoniae</td>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Fungi</td>
<td>Extracellular</td>
<td>2–200 µm</td>
<td>Candida albicans</td>
<td>Candida albicans</td>
<td>Candida albicans</td>
<td>Thrush</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Extracellular</td>
<td>1–50 µm</td>
<td>Trypanosoma gambiense</td>
<td>Trypanosoma gambiense</td>
<td>Sleeping sickness</td>
<td></td>
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<tr>
<td></td>
<td>Facultative intracellular</td>
<td></td>
<td>Trypanosoma cruzi</td>
<td>Trypanosoma cruzi</td>
<td>Trypanosoma cruzi</td>
<td>Chagas disease</td>
</tr>
<tr>
<td></td>
<td>Obligate intracellular</td>
<td></td>
<td>Leishmania donovani</td>
<td>Leishmania donovani</td>
<td>Leishmania donovani</td>
<td>Kala-azar</td>
</tr>
<tr>
<td>Helminths</td>
<td>Extracellular</td>
<td>3 mm–10 m</td>
<td>Wuchereria bancrofti</td>
<td>Wuchereria bancrofti</td>
<td>Wuchereria bancrofti</td>
<td>Filariasis</td>
</tr>
<tr>
<td></td>
<td>Intracellular</td>
<td></td>
<td>Trichinella spiralis</td>
<td>Trichinella spiralis</td>
<td>Trichinella spiralis</td>
<td>Trichinosis</td>
</tr>
</tbody>
</table>

Each group has distinctive characteristics (structural and molecular make-up, biochemical and metabolic strategies, reproductive processes) which determine how the organisms interact with their hosts and how they cause disease.

Brief Overview of Classes of Human Pathogens

Viruses

- Consist of RNA or DNA contained in a protein shell; some enveloped in lipid membrane
- Spectrum of illness
  - Cause acute, transient illnesses (colds, gastroenteritis)
  - Capable of lifelong latency and of long-term reactivation (herpes zoster) or of giving rise to chronic disease (Hepatitis B)
- Oncogenic (Human papillomavirus, Epstein-Barr virus)
Bacteria

• Unicellular; classified according to structural features of their envelope and whether they are capsulated or unencapsulated
• Capable of synthesizing own DNA, RNA and proteins but rely on host for favorable growth conditions
• Spectrum of illness
  • Low virulence to acute life threatening infections to chronic debilitating illness

Fungi

• Larger and more complex than bacteria
  • Growth patterns include budding yeast and slender tubes called hyphae
• Spectrum of illness
  • Infect superficial layers of skin (Tinea)
  • Deep fungal infections can spread systemically (some species limited to geographic regions eg. Blastomyces, Histoplasma, Coccidioides)
  • Opportunistic fungi that normally colonize the body may cause disease in immunosuppressed patients such as lethal pneumonia & tissue necrosis (Aspergillus, Cryptococcus)
Parasites

- Most complex microbes

Protozoa

- Parasitic, single-celled organisms with motility, pliable plasma membranes and complex cytoplasmic organelles
- Spectrum of illness
  - Invade, digest human tissues (Entamoeba histolytica)
  - Replicate in and kill cells (Plasmodia)
  - Damage tissue by inflammatory and immunologic responses (Trypanosomes)
  - Latent, reactivate in immunocompromised host (Toxoplasma gondii)
Helminths

- Parasitic WORMS
  - Highly differentiated multicellular organisms
  - Complex life cycles
    - Most are dependent on an intermediary host or vector for asexual reproduction
  - Roundworms (nematodes), Flatworms (trematodes), Tapeworms (cestodes)
  - Disease often caused by host inflammatory responses (ex. Schistosomiasis) and in proportion to the number of infecting organisms

Helminths - example

- Cestodes: gutless worms, heads sprout a ribbon of flat segments (tapeworms)
Prions

- Misfolded protein aggregates
  - Prion protein (PrP)
- Rare
- Aggregate in CNS
  - Causes of neurodegenerative diseases such as kuru, bovine spongiform encephalopathy (mad cow disease), Creutzfeldt-Jakob Disease (CJD)
- Transmitted person to person, by surgery, organ transplantation, blood transfusion
  - Highly resistant to normal methods of sterilization

Microbiome

- Microbial population that colonizes human body
  - Intestinal tract, skin, upper airway, vagina
- Most do not cause harm
  - May cause disease
- Increasing knowledge that microbiome plays roles in health and development
Patient Perspective

- What do patients (and their families) want to know when they are diagnosed with an “infection”?  
  - What is it?  
  - How did I get it?  
  - Why am I so sick?  
  - What is the treatment?  
  - When will I feel/get better?  
  - Can I get this again?  
  - What can I do to not get it again?  
  - Can I get it? (family, friends)

“How did I get it?”

Routes of Entry and Dissemination of Microbes

Robbins Figure 9.6

Portals of Entry of Microbial Infection

Robbins Table 9.6
Skin

- Dense keratin layer natural barrier to infection
- Low pH (<5.5) & fatty acids inhibit growth of microorganisms other than the normal flora
- Entry through breaks in the skin
  - Superficial pricks
  - Wounds
  - Burns
  - Diabetic and pressure-related foot sores
  - Intravenous catheters or devices
  - Needle sticks/injections
  - Insect or animal bite
  - Tattoos
- Only a few microorganisms able to traverse the unbroken skin
  - Schistosomal larvae released from freshwater snails penetrate swimmers’ skin by releasing enzymes that dissolve the extracellular matrix.
  - Certain fungi (dermatophytes) can infect intact stratum corneum, hair, and nails

Gastrointestinal Tract

- Infection via GI tract occurs when local defenses are weakened or organisms develop strategies to overcome these defenses
- Normal defenses:
  - Acid secretions
  - Layer of viscus mucus covering intestinal epithelium
  - Lytic pancreatic enzymes and bile detergents
  - Defensins = mucosal antimicrobial peptides
  - Normal flora
  - Secreted IgA antibodies— made by plasma cells located in mucus-associated lymphoid tissue (MALT)

- GI pathogens transmitted by food or drink contaminated with fecal material
  - Hygiene failure
  - Natural disasters – floods and earthquakes
  - Poor hand washing
  - Lack of sanitation infrastructure

Respiratory Tract

- Large numbers of viruses, bacteria, fungi inhaled
  - In dust or aerosol particles
  - Also via fine particles (travels into respiratory system is inversely proportional to their size)
  - Larger particles impacted or inactivated by lining nasal and upper respiratory tract
  - Microorganisms ingested – microvilli extend labeled cells transported by cilia action to back of the throat, where they are swallowed or phagocytosed by enteron or respiratory epithelium
  - Small particles (less than 5µm) may reach alveoli, where they are phagocytosed by alveolar macrophages or by macrophages recruited by cytokines

- Microorganisms that evade the normal healthy respiratory tract have developed specific mechanisms to overcome mucociliary defenses or to avoid destruction by alveolar macrophages

- Adhere:
  - Influenza virus possesses hemagglutinin proteins that project from surface of the virus and bind to sialic acid on surface of epithelial cells
  - Attachment induces the host cell to engulf the virus, leading to infection and replication within the host cell

- Release Toxins:
  - Haemophilus influenza, Mycoplasma pneumoniae, and Bordetella pertussis release toxins that impair ciliary activity

- Evasion System:
  - M. tuberculosis gains foothold in alveoli because it escapes killing within the phagolysosomes of macrophages
Urogenital Tract

- Almost always invaded from exterior by way of urethra
- Regular flushing of urinary tract with urine serves as defense against invading microorganisms
- Successful pathogens (e.g., N. gonorrhoeae, E. coli) adhere to urinary epithelium
- Anatomy plays important role in infection
  - Women >10X as many urinary tract infections than men
  - Distance between urinary bladder and skin (the length of the urethra)
  - Obstruction of urinary flow or reflux can compromise normal defenses and increase susceptibility to urinary tract infections

Dissemination (Spread) Within the Host

- Some proliferate locally at site of initial infection
  - V. cholerae stays confined to hollow intestine
  - Papillomavirus stays within epithelial cells
- Lysis and direct invasion
  - S. aureus secretes enzyme hyaluronidase - degrades extracellular matrix between host cells
- Spread through blood or lymphatics
  - Can spread either free in extracellular fluid or within host cells
  - Plasmodium (malaria) and Babesia carried within red blood cells
  - All helminths transported in plasma
- Cell to cell transmission
  - Most viruses spread locally cell to cell by replication and release of infectious virions
  - Some viruses propagate cell to cell causing fusion of cells
  - Some viruses transport within nerves (rabies virus, varicella-zoster virus)

Can I get it?

Release from the Body and Transmission of Microbes

- Transmission depends on hardness of microbe
  - Some microbes survive for extended periods in dust, food, or water
  - Less hardy microorganisms must be quickly passed from person to person, often by direct contact
- For transmission of disease, the mode of exit of microorganism from host's body as important as entry into it
  - Every fluid or tissue normally secreted, excreted, or shed is used by microorganisms to leave the host for transmission to new victims
Transmission of Microbes

Transmission of infections can occur by:
• contact (direct and indirect)
• respiratory droplets
• fecal-oral route
• sexual transmission
• urine
• vertical transmission from mother to fetus or newborn
• insect/arthropod vectors

“Why am I so sick?”
Summarize how microbes cause disease
Establishing Infection, Damaging Tissues

- Microbes may:
  1) Enter host cells and **directly cause death** of infected cells
  2) Cause **Indirect damage**
     - Release toxins
     - Kill cells at a distance
     - Release enzymes
     - Degrade tissue components
     - Damage blood vessels
  3) Induce **host immune responses**
     - Though response directed toward microbe, additional tissue damaged caused

- After bypassing host tissue barriers, infectious microorganisms must evade host innate and adaptive immunity mechanisms to successfully proliferate and be transmitted to the next host

- **Immune Evasion by Microorganisms**
  Strategies include:
  - Antigenic variation
  - Inactivating antibodies or complement
  - Resisting phagocytosis
  - Suppressing the host adaptive immune response
Mechanisms of Antigenic Variation

- To escape recognition, microbes use many strategies that involve genetic mechanisms for generating antigenic variation

Integration with Pathology Principles:
Patterns of Host Responses to Microorganisms in Tissue

Patterns of Host Responses to Microorganisms

- In normal (immunocompetent) persons, patterns of host responses are fairly stereotypical for different classes of microbes
- Response patterns can be used to infer possible causal organisms
  - Neutrophil-rich acute suppurative inflammation
  - Mononuclear Inflammation
  - Granulomatous inflammation
  - Cytopathic-Cytolymphoproliferative Reaction
  - Chronic inflammation and scarring
Suppurative (Purulent) Inflammation

- Typical of infections with many bacteria
  - "Pyogenic"
- Characterized by "pus"
  - Neutrophils, liquefied debris of necrotic cells, edema
- Abscess= localized collection of pus

Mononuclear Inflammation

- Diffuse, predominantly mononuclear infiltrates common feature of all chronic inflammatory processes
- May see during acute response to
  - Viruses, intracellular bacteria, or intracellular parasites
- Which mononuclear cell predominates within inflammatory lesion depends on host immune response to the organism
  - Lymphocytes in acute Hepatitis B infection
  - Plasma cells in the primary and secondary lesions of syphilis

Granulomatous Inflammation

- Distinctive form of mononuclear inflammation
- Usually evoked by infectious agents that resist eradication but nevertheless capable of stimulating strong T cell–mediated immunity
  - Commonly seen with Mycobacterium tuberculosis infection
    - Some fungi (Histoplasma capsulatum), Schistosome eggs
Cytopathic-Cytoproliferative Reaction

- Structural changes in host cells usually produced by viruses
- Lesions characterized by cell necrosis or cellular proliferation
  - usually sparse inflammatory cells
- Some viruses replicate within cells and make viral aggregates visible as inclusion bodies
  - Example = Cytomegalovirus

Intranuclear Inclusion
Cytoplasmic Inclusions

Chronic Inflammation and Scarring

- Many infections elicit chronic inflammation, which can resolve with complete healing or lead to extensive scarring
  - Example = Schistosoma haematobium infection of the bladder with numerous calcified eggs and extensive scarring

Patterns of Host Response

- Patterns of tissue reactions are useful guidelines for analyzing microscopic features of infectious processes
- In immunocompromised persons, the absence of a host inflammatory response frequently eliminates some of the histologic clues about the potential nature of infecting microorganism
Summary

- Classify common human pathogens within the appropriate Taxonomic Class
- Summarize routes of entry and dissemination of microbes
- Summarize modes of transmission of microbes
- Summarize means by which microbes may evade the host’s immune system
- Describe the spectrum of inflammatory responses to infection and classic examples of microbes that cause each response

Review Questions:

- Define “prion” and give examples of prion derived diseases
- Which class of microbe can be potentially seen with the naked eye?
- Give 2 examples of micro-organisms that elicit granulomatous responses
- Describe what happens when a microbe that is <5μm is inhaled vs a larger microbe
- Discuss factors which impact the development of an infection of the urinary tract
- List means by which microbes generate antigenic variation
- Define “viral inclusion body”