

MICROBIOLOGY 308

Paradigms in Bacterial Pathogenesis

M,W,F 12pm

Instructor: Dr. Rachel Fernandez

Textbook: Bacterial Pathogenesis: A Molecular Approach, 3rd Edition
by Wilson, Salyers, Whitt and Winkler. ISBN 9781555814182

Tentative Course Outline

1. Introduction to course

- Importance of Infectious Diseases
- Definition of a pathogen
- Koch's postulates

2. Summary of key concepts of bacterial cell surfaces and structures

- Importance of the cell membrane
- Biogenesis of peptidoglycan and the cell envelope

3. Antibiotics

- Brief overview on antibiotics
- Focus on antibiotics that affect the cell wall
- Beta-lactam antibiotic mechanism of action and resistance
- Glycopeptide antibiotics mechanism of action and resistance

4. Host defenses and microbial mechanisms for evasion

- Summary of key concepts in innate immunity (including NFkB signaling pathways as an example).
- Bacterial virulence factors that alter NFkB signaling
- Complement pathway
- Evasion of complement
- Phagocytosis (oxidative burst, oxygen-dependent and oxygen independent killing)
- Mechanisms to combat phagocytic killing
- Summary of adaptive immunity
- Overview of bacterial mechanisms to avoid immune detection

5. Vaccines

- Overview of vaccines from history to practical considerations both locally and globally
- Designing vaccines (killed or attenuated, whole-cell or subunit, reverse vaccinology, adjuvants)
- Practical example of the *H. influenzae* B conjugate vaccine
- DNA vaccines
- How to deal with bacteria that have multiple serotypes

6. Techniques for studying bacterial pathogens & their virulence factors

- Overview of models –advantages, drawbacks, limitations
- Koch's postulates –molecular version
- Gain of function/Loss of function experiments (advantages, limitations)
- Signature-tagged mutagenesis
- Promoter traps (in vivo expression technology (IVET) and differential fluorescence induction (DFI)
- Hybridization-based experiments (subtractive hybridization, microarrays)

7. Selected mechanisms of pathogenesis

- **Adherence**
 - Overview of ligands (afimbrial and fimbrial adhesins) and receptors
 - Direct binding vs binding to extracellular matrix proteins
 - Brief description of urinary tract infections, and the importance of adherence
 - Biogenesis of the pap-pilus
- **Invasion**
 - Overview of invasion mechanisms –zipper vs. trigger
 - Brief description of Yersinia infections, and mechanism of zipper-mediated uptake by invasin.
 - Importance of integrins, actin polymerization
 - Brief description of Shigella infections and mechanism of trigger mediated uptake.
- **Intracellular Survival**
 - Brief overview of intracellular survival mechanisms (eg within professional phagocytes)
 - Focus on inhibition of phagosome-lysosome fusion (or remodeling of phagosome membrane) using Legionella and Chlamydia (or Salmonella, or Mycobacteria) as specific examples, and escape from phagosome into the cytoplasm using Listeria and Shigella as examples.
 - Identification of both bacterial and host components where known.

- **Toxins**
 - Brief overview (concept of A-B toxins)
 - Cytolytic toxins .
 - Describe the mechanisms of enzymatic vs. non-enzymatic (ie pore-formers) toxins
 - Cytotoxic toxins.
 - Describe the mechanisms of toxins that
 - inhibit protein synthesis (Diphtheria toxin and Pseudomonas exotoxin A, shiga toxin)
 - interfere with signal transduction (cholera toxin, pertussis toxin)
 - interfere with actin polymerization (*C. difficile* toxins A and B)
 - proteases (neurotoxins tetanus toxin, botulinum toxin)
 - Anthrax toxin (unusual A-B toxin; how to inhibit its function)

8. Evolution of pathogens

- Pathogenicity Islands and phages
- General overview of how these are identified
- Impact of phages and pathogenicity islands on virulence (*V. cholerae*, *Staphylococci* as examples)

9. Tying it all together

- Seminars on the molecular mechanisms of pathogenesis for select bacteria