Antimicrobial Drugs - Early History

- Paul Erlich identifies salvarsan for localized control of syphilis
- Sulfanilamides, synthetic compounds, are the first systemic antimicrobial drugs
- 1928 - Alexander Fleming identifies penicillin, an antimicrobial drug produced by a fungus
- Selman Waksman discovers streptomycin, defines antibiotic as a compound produced by a microorganism that inhibits growth of other microorganisms

Availability of antimicrobial drugs varies with target phylogeny

- Numerous antibacterial drugs target significant differences between prokaryotic and eukaryotic cells
- Antifungal, antiprotozoal and antihelminthic drugs are limited by similarity of these cells to ours
- Antiviral drugs must target limited number of virus-specific enzymes or attachment proteins
Spectrum of Activity

- **Broad spectrum** drugs are *microbicidal or microbistatic* for a wide range of microorganisms
  - Advantage: Treatment of infection before identification of agent
  - Disadvantages
    - Damage to normal flora
    - Selection of resistance among normal flora
- **Narrow spectrum** drugs affect a limited range of microorganisms
  - Advantages
    - Less damage to normal flora
    - Less selection for resistance
  - Disadvantage: Requires knowledge of identity of infectious agent

Antibacterial Targets

**Antibacterial Drugs that Target the Cell Wall**

- **β-lactams**, including the penicillins and cephalosporins
- **Glycopeptides**, including **vancomycin**
- **Isoniazid** and **ethambutol** for mycobacterial infections
- **Bacitracin**, limited to topical application
Penicillins and Cephalosporins

- Inhibitors of peptidoglycan synthesis
- Share a common β-lactam ring structure
- Modifications allow variation in availability and target range

Bacteria may produce β-lactamase
Antimicrobial Drugs Targeting Protein Synthesis

- **Aminoglycosides** - Kanamycin, Tobramycin, Gentamicin, etc.
- **Tetracyclines** - Oxycycline, Minocycline, etc.
- **Macrolides**, including Erythromycin
- **Chloramphenicol**

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**Tetracyclines**
Antimicrobial Drugs that Target Nucleic Acid Synthesis

- **Rifamycins**, including *rifampicin*, interfere with prokaryotic RNA synthesis
- **Quinolones** and *fluoroquinolines* interfere with prokaryotic DNA replication
(a) Adenine nucleosides

(b) Thymine nucleosides

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