Chapter 10, part A
Antimicrobial Drugs
Antimicrobial Drugs

- **Chemotherapy**: The use of drugs to treat a disease
- **Antimicrobial drugs**: Interfere with the growth of microbes within a host
- **Antibiotic**: Substance produced by a microbe that, in small amounts, inhibits another microbe
- **Selective toxicity**: A drug that kills harmful microbes without damaging the host
• 1928 – Fleming discovered penicillin, produced by *Penicillium*.

• 1940 – Howard Florey and Ernst Chain performed first clinical trials of penicillin.
<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Antibiotic</th>
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<tbody>
<tr>
<td><strong>Gram-Positive Rods</strong></td>
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<tr>
<td><em>Bacillus subtilis</em></td>
<td>Bacitracin</td>
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<td><em>Bacillus polymyxa</em></td>
<td>Polymyxin</td>
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<td><strong>Actinomycetes</strong></td>
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<tr>
<td><em>Streptomyces nodosus</em></td>
<td>Amphotericin B</td>
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<tr>
<td><em>Streptomyces venezuelae</em></td>
<td>Chloramphenicol</td>
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<td><em>Streptomyces aureofaciens</em></td>
<td>Chlortetracycline and tetracycline</td>
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<td><em>Streptomyces erythraeus</em></td>
<td>Erythromycin</td>
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<td><em>Streptomyces fradiae</em></td>
<td>Neomycin</td>
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<td><em>Streptomyces griseus</em></td>
<td>Streptomycin</td>
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<td><em>Micromonospora purpureae</em></td>
<td>Gentamicin</td>
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<td><strong>Fungi</strong></td>
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<tr>
<td><em>Cephalosporium spp.</em></td>
<td>Cephalothin</td>
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<tr>
<td><em>Penicillium griseofulvum</em></td>
<td>Griseofulvin</td>
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<td><em>Penicillium notatum</em></td>
<td>Penicillin</td>
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<td>Mycobacteria*</td>
<td>Prokaryotes</td>
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*Growth of these bacteria frequently occurs within macrophages or tissue structures.
†Obligately intracellular bacteria.
The Action of Antimicrobial Drugs

- Broad-spectrum
- Superinfection
- Bactericidal
- Bacteriostatic
The Action of Antimicrobial Drugs

- **Inhibition of cell wall synthesis:** Penicillins, cephalosporins, bacitracin, vancomycin
- **Inhibition of protein synthesis:** Chloramphenicol, erythromycin, tetracyclines, streptomycin
- **Inhibition of nucleic acid replication and transcription:** Quinolones, rifampin
- **Injury to plasma membrane:** Polymyxin B
- **Inhibition of synthesis of essential metabolites:** Sulfanilamide, trimethoprim

**Figure 20.2**
The Action of Antimicrobial Drugs

(a) Three-dimensional detail of the protein synthesis site showing the 30S and 50S subunit portions of the 70S prokaryotic ribosome.

(b) In the diagram the black arrows indicate the different points at which chloramphenicol, erythromycin, the tetracyclines, and streptomycin exert their activities.
Antibacterial Antibiotics
Inhibitors of Cell Wall Synthesis

• Penicillin
  • Natural penicillins
  • Semisynthetic penicillins
Penicillins

(a) Natural (antibiotic) penicillins

Penicillin G (Requires injection)

Penicillin V (Can be taken orally)

(b) Semisynthetic penicillins

Oxacillin (Resistant to penicillinase)

Ampicillin (Extended spectrum)
Antibacterial Antibiotics
Inhibitors of Cell Wall Synthesis

- Penicillin
  - Penicillinase-resistant penicillins
  - Extended-spectrum penicillins
  - Penicillins + \( \beta \)-lactamase inhibitors
  - Carbapenems
  - Monobactam
Antibacterial Antibiotics
Inhibitors of Cell Wall Synthesis

Figure 20.8
Cephalosporins

- 2\textsuperscript{nd}, 3\textsuperscript{rd}, and 4\textsuperscript{th} generations more effective against gram-negatives
Antibacterial Antibiotics
Inhibitors of Cell Wall Synthesis

- Polypeptide antibiotics
  - Bacitracin
    - Topical application
    - Against gram-positives
  - Vancomycin
    - Glycopeptide
    - Important "last line" against antibiotic resistant *S. aureus*
Antimycobacterium antibiotics

- Isoniazid (INH)
  - Inhibits mycolic acid synthesis
- Ethambutol
  - Inhibits incorporation of mycolic acid
Antibacterial Antibiotics
Inhibitors of Protein Synthesis

- Chloramphenicol
  - Broad spectrum
    - Binds 50S subunit, inhibits peptide bond formation
- Aminoglycosides
  - Streptomycin, neomycin, gentamycin
    - Broad spectrum
      - Changes shape of 30S subunit
Antibacterial Antibiotics
Inhibitors of Protein Synthesis

- Tetracyclines
  - Broad spectrum
    - Interferes with tRNA attachment
- Macrolides
  - Gram-positives
    - Binds 50S, prevents translocation
- Erythromycin
  - Gram-positives
    - Binds 50S, prevents translocation
Antibacterial Antibiotics
Inhibitors of Protein Synthesis

- Streptogramins
  - Gram-positives
    - Binds 50S subunit, inhibits translation
- Synercid
  - Gram-positives
    - Binds 50S subunit, inhibits translation
- Oxazolidinones
  - Linezolid
    - Gram-positives
      - Binds 50S subunit, prevents formation of 70S ribosome
Antibacterial Antibiotics
Injury to the Plasma Membrane

• Polymyxin B
  • Topical
  • Combined with bacitracin and neomycin in over-the-counter preparation
Antibacterial Antibiotics
Inhibitors of Nucleic Acid Synthesis

- Rifamycin
  - Inhibits RNA synthesis
  - Antituberculosis
- Quinolones and fluoroquinolones
  - Ciprofloxacin
  - Inhibits DNA gyrase
  - Urinary tract infections
Antibacterial Antibiotics
Competitive Inhibitors

- Sulfonamides (Sulfa drugs)
  - Inhibit folic acid synthesis
  - Broad spectrum