I. History and development of antimicrobial drugs (section 21.1)
   a. Erlich-magic bullet - p. 469 (A glimpse of history)
   b. Discovery of antibiotics
      i. Fleming - discovered penicillin
      ii. Chain and Florey - first to purify penicillin

II. Features of antimicrobial drugs (section 21.2)
   a. Selective toxicity
      i. Target (figure 21.2)
      ii. Therapeutic index - lowest dose toxic to the patient / dose used therapeutically
   b. Antimicrobial action
      i. Bacteriostatic
      ii. Bactericidal
   c. Spectrum of activity
      i. Broad-spectrum
      ii. Narrow-spectrum
   d. Tissue distribution/metabolism/excretion
   e. Adverse effects
      i. Allergic reactions
      ii. Toxic effects
      iii. Suppression of normal flora
   f. Resistance
      i. Intrinsic/innate
      ii. Acquired
   g. Cost

III. Example - Antibacterial medications that inhibit cell wall synthesis (p. 475 - 476)
   a. β-lactam drugs - penicillin G as an example
   b. Target-peptidoglycan synthesis
   c. Family of penicillins
      i. Natural penicillins
      ii. Penicillinase-resistant penicillins
      iii. Broad spectrum penicillins
      iv. Penicillins + β-lactamase inhibitor

IV. Example – Antibacterial medication that inhibits a biosynthetic pathway (p. 478-479)
V. Example – Antiviral medications (p.486-488)
   a. Nucleotide and nucleotide analogs
   b. Enzyme inhibitors

VI. Determining the susceptibility of a bacterial strain to an antimicrobial drug (section 21.4)
   a. Minimum inhibitory concentration (MIC) (figure 21.9)
      - Disk diffusion (Kirby-Bauer test) (figure 21.10)
      - Mechanisms of resistance (figure 21.14)
   b. Disk diffusion (Kirby-Bauer test) (figure 21.10)
   c. Mechanisms of resistance (figure 21.14)
      - Acquisition of resistance
        i. Single step
           1. S to R
           2. Solution – combination therapy
ii. Multi-step
   1. S decreasing stepwise to R
   2. Solution – patient compliance

e. Examples of emerging antimicrobial resistance
   i. *Neisseria gonorrhoea*
   ii. *Enterococcus* species
      1. Intrinsically less susceptible
      2. VRE: vancomycin-resistant enterococci
   iii. *Staphylococcus aureus*
      1. MRSA: methicillin-resistant *Staphylococcus aureus*
      2. VRSA: vancomycin-resistant *Staphylococcus aureus*
   iv. *Streptococcus pneumoniae*
   v. *Mycobacterium tuberculosis*
      1. MDR-TB
      2. XDR-TB

f. Slowing the emergence and spread of antimicrobial resistance
   i. Responsibilities of physicians and other health care workers e.g. prescribe antimicrobial
      medications only when appropriate
   ii. Responsibilities of patients e.g. take medications as prescribed
   iii. Importance of an educated public e.g. antibiotics are NOT effective against viruses
   iv. Global impacts of the use of antimicrobial drugs e.g. animal feed

VII. Study Questions
1. List 4 targets of selective toxicity of antimicrobial drugs.
2. Which would be safer, a drug with a therapeutic index of 2 or one with a therapeutic index of 100?
3. Describe a situation when a bactericidal drug would be more appropriate than a bacteriostatic drug.
4. Describe a situation when a broad-spectrum drug would be most suitable.
5. Describe a situation when a narrow-spectrum drug would be most suitable.
6. Describe the benefits of a drug that has a longer half-life versus a shorter half-life.
7. What is antibiotic-associated colitis?
8. Drugs that have which target would be expected to be the least toxic?
9. *Mycoplasma* species are intrinsically resistant to penicillin. Why?
10. Why is penicillin not effective against most Gram-negative bacteria?
11. Why is penicillin not effective against most *Staphylococcus aureus* strains?
12. What is the key characteristic of each group in the “family of penicillins”?
13. How is the MIC of a strain determined?
14. What does the Kirby-Bauer test indicate?
15. What four general mechanisms allow a cell to resist the effects of an antimicrobial drug?
16. In the case of certain antibiotics, a single point mutation allows a bacterial cell to become resistant to
    the drug. What can be done to prevent this type of resistance?
17. In the case of many antibiotics, several different mutations must occur for a bacterial cell to become
    resistant to the drug. What can be done to prevent this type of resistance?