Chapter 21 Antimicrobial Medications

Summary Outline

21.1 History and development of antimicrobial drugs
- A. Definitions
  1. **Chemotherapeutic agents** are chemicals used as therapeutic drugs.
  2. **Antimicrobial drugs** (antimicrobials) are chemotherapeutic agents that are effective against microbial infections.
  3. **Antibiotics** are antimicrobial chemicals that are naturally produced by microorganisms.
- B. The development of **Salvarsan** by Paul Ehrlich was the first documented example of an antimicrobial medication.
- C. Alexander Fleming discovered that the fungus *Penicillium* produces **penicillin** that kills some bacteria.
- D. **Antimicrobial drugs** can be **chemically modified** to give them new properties. **Penicillin** has been altered to create a **family of drugs** with a variety of new characteristics.

21.2 Features of antimicrobial drugs
- A. Most modern **antibiotics** come from the bacteria ***Streptomyces*** and ***Bacillus*** and the eukaryotic fungi ***Penicillium*** and ***Cephalosporium***.
- B. Medically useful antimicrobials are **selectively toxic**. The relative toxicity of a drug is expressed as the **therapeutic index**, which is the lowest dose toxic to the patient divided by the dose typically used for therapy.
- C. Antimicrobial action
  1. **Bacteriostatic drugs inhibit the growth of microorganisms**.
  2. **Drugs that kill microorganisms are bactericidal**.
- D. Spectrum of activity
  1. **Broad-spectrum** antimicrobials affect a wide range of bacteria.
  2. Those that affect a narrow range are called **narrow-spectrum**.
- E. Tissue distribution, metabolism and excretion of the drug
  1. Some **antimicrobials cross the blood brain barrier** into the CSF; these can be used to treat meningitis.
  2. **Drugs that are unstable in acid** cannot be taken orally and therefore must be administered through **injection**.
  3. **Drugs that have a long half-life** need to be administered **less frequently**.
- F. **Synergistic combinations** of drugs result in **enhanced antimicrobial activity**.
- G. **Antagonistic antimicrobials interfere** with the activity of others.
- H. Combinations are neither synergistic nor antagonistic are called **additive**.
- I. Adverse effects include **allergies** to antimicrobials, **side effects** and **alteration of the normal flora**.
- J. **Resistance** to antimicrobials is intrinsic or innate. Microorganisms can develop resistance through **spontaneous mutation** or the **acquisition of new genetic information**.

21.3 **Mechanisms of action** of antimicrobial drugs
- A. **Antimicrobial drugs** target bacterial processes that utilize enzymes or structures that are either different, absent or not commonly found in eukaryotic cells.
- B. Antibacterial medications that **inhibit cell wall synthesis**
  1. The **β-lactam drugs** (**penicillins, cephalosporins, carbapenems** and **monobactams**) irreversibly **inhibit penicillin-binding proteins** (PBPs), ultimately leading to **cell lysis**. These drugs differ in their **spectrum of activity**.

2. **Vancomycin** blocks peptidoglycan synthesis.
3. **Bacitracin** interferes with the transport of peptidoglycan precursors.

C. Antibacterial medications **that inhibit protein synthesis**
1. The **prokaryotic 70S ribosome** serves as a target for selective toxicity.
2. Antibiotics include **aminoglycosides**, **tetracycline**, **macrolides**, **chloramphenicol**, **lincosamides**, **oxazolidinones** and **streptogramins**.

D. Antibacterial medications that **inhibit nucleic acid synthesis**
1. The **fluoroquinolones** interfere with DNA replication and transcription.
2. The **rifamycins** block initiation of transcription.

E. Antibacterial medications that **inhibit metabolic pathways**: **Sulfa drugs** and **Trimethoprim** inhibit enzymes.

F. Antibacterial medications that **interfere with cell membrane function**: **Polymyxin B** damages bacterial membranes.

G. Antibacterial medications that **interfere with processes essential to *Mycobacterium tuberculosis***. Medications include **isoniazid**, **ethambutol** and **pyrazinamide.**

21.4 **Determining** the **sensitivity** of a bacterial strain to an antimicrobial drug

A. Determining the **minimum inhibitory concentration (MIC)** and **bactericidal concentrations (MBC)**

B. The **Kirby-Bauer disc diffusion test** is routinely used to qualitatively **determine the susceptibility** of a given organism to antimicrobial drugs.

C. **Antimicrobial susceptibility** can be determined by **automated methods** and the **E test** can be used to **determine the MIC**.

21.5 **Resistance** to antibacterial drugs

A. As antimicrobials are increasingly used and misused, the bacterial strains that are resistant to their effects have a selective advantage over their sensitive counterparts.

B. **Mechanisms** of resistance include **enzymes** that chemically modify a drug, **structural changes** in the target, **altered porin proteins** and **efflux pumps**.

C. **Vertical evolution** is the acquisition of resistance through **spontaneous mutation**.

D. **Horizontal evolution** is the acquisition of resistance through **gene transfer**.

E. The most common **mechanism of transfer of antibiotic resistance genes** is through the **conjugative transfer of R plasmids**.

F. The **emergence** and **spread of antimicrobial resistance can be slowed** by physicians **prescribing antimicrobials appropriately**, by patients carefully **following instructions** when taking antimicrobials and by **educating** the public about the appropriateness and limitations of antimicrobial therapy.

21.6 **Mechanism of action of antiviral drugs**

A. **Viruses use host cell machinery**, making them **difficult targets** for **selective toxicity**. There are **few antiviral drugs available** and they are generally **effective against only a specific type of virus**; none are able to eliminate latent viruses.

B. **Amantadine and rimantadine block** the **uncoating** of influenza A virus after it enters a cell.

C. **Nucleic acid synthesis**: **Nucleotide analogs interfere with replication** when they are incorporated into viral DNA.

D. **Protease inhibitors inhibit protease**, the enzyme required for the production of infectious HIV particles.

E. **Neuraminidase inhibitors** interfere with the release of influenza virus from a host cell.

21.7 **Mechanism of action of antifungal drugs: Few targets** for selectively toxic antifungal drugs.

A. Antifungal drugs that **inhibit plasma membrane synthesis and function** include **polyenes, azoles** and **allylamines**.

B. **Griseofulvin inhibits fungal cell division**.

C. **Flucytosine inhibits nucleic acid synthesis** and is used for **systemic yeast infections**.

21.8. Most **antiparasitic drugs** are thought to **interfere** with **biosynthetic pathways** of protozoan parasites or the neuromuscular function of worms.