







Chapter 20 Antimicrobial Drugs

"Magic Bullet" - Paul Ehrlich provided the basis for chemotherapy, he suggested that there might be a chemical (drug) that would selectively find and destroy pathogens with out harming the host.

Antibiotics - a substance that is produced by microorganisms which inhibits the growth of other microorganisms. The first person to notice this was Alexander Fleming. **Based on this definition synthetic drugs like sulfa drugs are technically not antibiotics.

"How well do they work?"

The spectrum of microbial activity refers to the drugs range of microbes that it effects.

- 1. Narrow-spectrum antibiotics have a small number of bacteria that they are effective against.
- 2. Broad-spectrum antibiotics have a large (broad) number of bacteria that they are effective against.

Factors required for the success of antibiotics:

- 1. Proper route of administration.
 - a. topical
 - b. oral
 - c. intramuscular
 - d. intravenous
- 2. Maintaining proper levels (concentrations) at the site of the infection.

Methods of Action of Antibiotics:

- 1. Inhibition of cell wall synthesis
 - a. penicillins (natural and semisynthetic)
 - b. cephalosporins
 - c. antimycobacterial
- 2. Inhibition of cell membrane function
 - a. polymyxin B
- 3. Inhibition of protein synthesis
 - a. chloramphenicol
 - b. aminoglycosides
 - c. tetracyclines
 - d. macrolides
 - e. streptogramins (synercid)
- 4. Inhibition of DNA and RNA synthesis
 - a. Rifampin
 - b. Quinolones and fluoroquinolones
- 5. Inhibition of metabolic processes
 - a. sulfonomides

Bacteriostatic drugs (inhibit but don't kill)

- Chloramphenical broad spectrum binds to a receptor site on the 50S subunit of the bacterial ribosome, inhibiting peptidyl transferase
- Macrolides gram positives bind to the 50S ribosomal subunit with a specific target in the 23S ribosomal RNA molecule and various ribosomal proteins
- · Clindamycin binding to the 50S rRNA of the large bacterial ribosome subunit
- Sulfonamides broad spectrum interfere with folic acid synthesis by preventing addition of paraaminobenzoic acid (PABA) into the folic acid molecule through competing for the enzyme dihydropteroate synthetase
- Trimethoprim interrupts the thymidine synthesis pathway, thus inhibiting DNA synthesis
- Tetracyclines broad spectrum inhibiting the binding of aminoacyl-tRNA to the mRNA-ribosome complex
- Tigecycline broad spectrum binds to 30S ribosomal subunit blocking tRNA from the A site
- Linezolid gram positive bacteria binds to the 50S subunit preventing formation of the initiation complex for protein synthesis
- Quinupristin/dalfopristin (synercid) Dalfopristin has been shown to inhibit the early phase of protein synthesis while quinupristin inhibits the late phase of protein synthesis

Bacteriocidal drugs (lethal)

- Aminoglycosides broad spectrum bind to the 30s ribosomal sub-unit and cause a misreading of the genetic code
- Beta-lactams (including cephalosporins) broad spectrum (though not used for many streps) interfere
 with the biosynthesis of the bacterial cell wall by binding to penicillin binding proteins (PBPs) that are
 located in the cell wall which leads to the inhibition of peptidoglycan synthesis which leads to cell
 death
- Vancomycin gram positive bacteria binds to precursors of the cell wall inhibiting cell wall synthesis, also inhibits RNA synthesis
- · Daptomycin *proposed* inhibition of lipoptechoic acid biosynthesis
- Tercoplanin inhibits cell wall synthesis
- Fluoroquinolones broad spectrum inhibit DNA synthesis by binding to the enzyme-DNA complex
- Rifampin treatment of TB binds to the active site of RNA polymerase
- Metronidazole anaerobes and protozoans inhibits nucleic acid synthesis by disrupting the DNA of microbial cells

Methods of testing susceptibility: (in vivo - living, in vitro - in glass)

- Diffusion method: a disc or strip is impregnated with the antibiotic to be studied, the disc is then applied
 to a Mueller Hinton plate that has been inoculated with the organism. Susceptibility is then determine
 based on the size of the zone of inhibition.
 - Kirby-Bauer Method discs, the zone of inhibition is determined by measuring the diameter of the area free from growth around the disc.
 - b. E-Test a plastic strip is used on the Mueller Hinton plate. The plastic strip has a calibrated amount of the antibiotic along its edge. It will form a tear drop shape and read as a MIC (minimum inhibitory concentration) at the base of the tear drop.
- Broth Dilution Tests: MIC established by inoculating bacteria into preset broths that have a decreasing (graduated) concentration of the bacteria. MIC values are determined by observing each broth for growth, the lowest well containing no growth is considered the MIC value.

Standard or Universal Precautions

PPE - personal protective equipment

WHO - World Health Organization

CDC - Center for Disease Control

Infectious Disease Doctor – specializes in the treatment of highly contagious diseases or hard to treat diseases.

Infection Control Nurse – responsible for ensuring the use of PPE, keep the data of nosocomial infections, putting into use and designing methods to decrease the number of nosocomial infections and keeps track of employee exposure.