Antimicrobial Drugs
(Chapter 20)
Lecture Materials
for
Amy Warenda Czura, Ph.D.
Suffolk County Community College
Eastern Campus

Primary Source for figures and content:

Antimicrobial drugs = both antibiotics and synthetic chemotherapy
Spectrum of microbial activity = range of microbial types affected by particular antimicrobial
e.g Penicillin → Gram +
(Gram negative more resistant in general: outer membrane only allows substances through porins, drug has to be small to pass)

Broad spectrum “antibiotics”:
-work on wide range of bacteria
-tend to kill off normal flora/microbiota
-can lead to superinfection:
Superinfection = one remaining organism takes over and causes disease, usually multi-drug resistant
Antibacterial drugs are
1. Bactericidal = kill bacteria directly
2. Bacteriostatic = prevent bacterial growth so host immune defenses can kill it

Selective toxicity = kill pathogen without harming host
Chemotherapy = treatment with chemical substances
Antibiotic = substance produced by microbes that inhibits or kills other microbes
First: Penicillin, Fleming 1928
Antibiotic producers:
Streptomyces species
Bacillus species
Penicillium
Cephalosporium

Modes of Action of Antibacterial Drugs:
*best drugs target bacterial specific feature so toxicity to humans is low
1. Inhibition of cell wall synthesis
   -peptidoglycan not found in humans
   -can inhibit NAG and NAM synthesis or crosslinking
   -only affects actively growing cells: new walls thin and weak

2. Inhibition of protein synthesis
   -eukaryotes = 80s ribosome, prokaryotes = 70s
   -can target 70s but toxicity to mitochondria
   -inhibit peptide bond formation, attachment of tRNA, or cause misreading of mRNA
3. Injury to plasma membrane
-alter permeability = loss of metabolites
-all membranes similar: toxicity risk

Tests to guide chemotherapy:
-different species have different susceptibilities
-resistance can appear over time
-must choose right drug in right concentration
1. Disk-diffusion/Kirby-Bauer test
-to determine which drug microbe is most susceptible to method:
-plate lawn of bacteria
-place disks of known antimicrobials on lawn
-read minimum level that inhibits growth

4. Inhibition of nucleic acid synthesis
-interfere with DNA replication or transcription
-all cells similar enzymes and nucleotides: toxicity risk

5. Inhibit synthesis of essential metabolites
-drug = competitive inhibitor of enzyme in metabolite synthesis pathway
-metabolite = any organic needed for growth
-must target bacterial specific pathways

2. E-test
-to estimate MIC (minimal inhibitory concentration) for effective dose method:
-plate lawn
-apply strip with concentration gradient of antimicrobial
3. Broth Dilution Test
-to determine MIC and MBC (minimal bactericidal concentration)
-differentiate bacteriocidal versus bacteriostatic drug action method:
-create sequence of decreasing concentration of drug in broth
-inoculate test bacteria
-test no growth wells for live bacteria in drug free media: growth = static (MIC)
 no growth = cells dead = cidal (MBC)

Mechanisms of Drug Resistance
1. destruction/inactivation of drug
2. prevent penetration to target site in cell
3. alteration of drug target site
4. rapid efflux (pump out of cell before drug finds target)

*resistance is passed on plasmids: gene to produce protein that will do one of the above, (typically mechanism #1 or 4)

Common Drugs (on handout)

[Image of drug resistance mechanisms]