

Antibiotics

Substances produced by a microorganism that (at low concentration) inhibit or kill other microorganisms

Talking about chemicals produced by living organisms that can kill or inhibit

BASICALLY: life destroys life

Chemotherapy

The use of drugs to treat a disease

Antimicrobial Drugs

Any substance of natural, synthetic or semi-synthetic origin that kills or inhibits the growth of a microorganism

Causes little or no host damage

Selection of Antimicrobial Agents

Requires knowing the following:

- The organism's identity
- The organism's susceptibility to a particular agent
- The site of infection
- Patient's factors
- The safety of the agent
- The cost of therapy

Selective Toxicity

Definition: Ability to kill or injure an invading microorganism without harming the cells of the host

LD50 Lethal dose at 50%; should be high

MIC Minimal inhibitory concentration; should be low; the lowest concentration of antibiotic that INHIBITS bacterial growth; lowest concentration that will stop the growth of bacteria

Selective Toxicity (cont)

MBC Minimal bactericidal concentration; should be; minimum concentration of antibiotic that KILLS the bacteria

Mechanism of Selective Targeting

Selective Toxicity: goal of antimicrobial drug therapy

Example: inhibit pathways or targets critical for pathogen survival at drug concentrations lower than those required to affect host pathways

Types of Pathways

Unique Pathways Also known as Cell Wall Synthesis Inhibitors; drug that inhibits the cell wall synthesis in microbes; the walls will lyse and the bacteria will die

Selective Pathways Also known as protein synthesis inhibitors

Common Pathways Also known as metabolites

Types of Antibiotic Agents

Type	Example
Cause inhibition of cell wall synthesis	Beta-Lactams
Alter the function of the cytoplasmic membrane; destroy cytoplasmic membranes	Isoniazid
Inhibit protein synthesis	Macrolides
Inhibit nucleic acid synthesis	Quinolones
Inhibit metabolite activity	Sulfonamides

Chemotherapeutic Spectra of Antibacterial Agents

Narrow Spectrum	Preferentially active against single or limited group of microorganisms Tx eg: isoniazid
Extended Spectrum	Effective against gram-positive and SOME gram negative bacteria Tx eg: ampicillin
Broad Spectrum	Active against BOTH gram positive and gram negative bacteria Tx eg: tetracycline Tx eg: chloramphenicol

Site of Action of Antibacterial Drug Classes

Cell Wall Inhibitors	Fosfomycin Cycloserine Vancomycin Penicillin Cephalosporins Monobactams Carbapenems Ehambutol Pyrazinamide Isoniazid
DNA Synthesis & Integrity Inhibitors	Sulfonamides Trimethoprim Quinolones
Transcription & Translation Inhibitors	Rifampin Aminoglycosides Spectinomycin Tetracyclines Macrolides Chloramphenicol Streptogramins Oxazolidinones



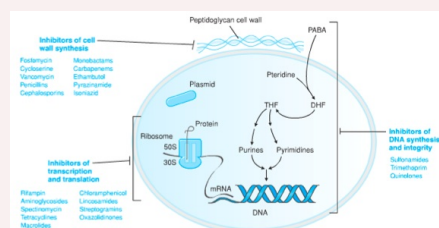
By heatherisawesome
(xoxheather_)

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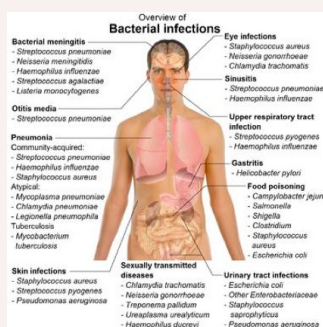
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Site of Action of Antibacterial Drug Classes



Types of Bacterial Infections



Bacteriostatic Drugs

INHIBIT the growth of pathogens without causing cell death

Eg: sulfonamides (DNA synthesis & intercity inhibitor)

Eg: chloramphenicol (transcription & translation inhibitor)

Bacteriostatic effectiveness relies on an intact host immune system to **CLEAR THE NONGROWING** (but viable) bacteria

Bactericidal Drugs

KILL BACTERIA

Eg: penicillin (cell wall inhibitor)

Eg: streptomycin (transcription and translation inhibitor)

Eg: give this to patients with AIDS because they don't have immunity

Bacteria Morphology

Spirilla Spiral shaped bacteria

Bacilla Rod shaped bacteria

Cocci Spherical shaped bacteria

Diplo- Pair

Staphylo- Clusters

Strepto- Chain

Gram POSITIVE Bacteria

Looks violet or dark blue in gram staining

Retains the crystal violet stain

Single layered membrane -- it lacks the second outer phospholipid bilayer

Thick layer of peptidoglycan -- only this forms the cell wall

Easier to treat with antibiotics because it only has one phospholipid bilayer

Gram NEGATIVE Bacteria

Don't retain crystal violet dye from gram staining

They are pink or red colored

Thin peptidoglycan wall

Two phospholipid bilayers (two membranes)

Consist of outer membrane and thin peptidoglycan wall as cell wall

The cell wall is thinner than gram positive

This is harder to treat with antibiotics because it has two phospholipid bilayers

Acid-Fast Bacteria

Definition: bacteria which resist decolorization with an acid-alcohol mixture during the acid-fast stain procedure

It retains the initial dye (carbofuchsin)

Acid-fast bacteria (mycobacteria and some of the related actinomycetes) appear red

Medically Important Microorganisms

Gram Positive Cocci

Gram Positive Bacilli

Gram Positive Cocci

Gram Negative Bacilli

Anaerobe Organisms

Spirochetes

Mycoplasma

Chlamydia

Other

Purpose of Using Single Drug to Treat a Patient

Reasons to Use Single Treatment Instead of Combinations of Antimicrobial Drugs

1. Reduces the possibility of superinfection
2. Reduces the emergence of resistant organisms
3. Minimizes toxicity

Combinations of Antimicrobial Drugs

Advantage: Synergism
Eg: beta-lactams and aminoglycosides

Disadvantage: Drug antagonism
Eg: combining bacteriostatic drug with bactericidal drug
Eg: giving a patient tetracycline with penicillin or cephalosporins

BASICALLY: Don't combine bacteriostatic drugs with bactericidal drugs

Prophylactic Antibiotics

- Use of antibiotics for prevention instead of treatment of infection
- May cause resistance and superinfection
- Use is limited

Complications of Antibiotic Therapy

1. Hypersensitivity
2. Direct toxicity
3. Superinfection

Antimicrobial Resistance

Definition: relative or complete lack of effect of antimicrobial against a previously susceptible microbe

Increase in MIC (remember MIC is lowest concentration needed to inhibit bacterial growth)

May be innate (an escape from antibiotic effect)

OR it may be acquired

Result of Acquired Antibiotic Resistance

1. Spontaneous, random chromosomal mutations. The mutations are due to change in either a structural protein receptor for an antibiotic or a protein involved in drug transport

2. Extrachromosomal transfer of drug-resistant genes

2a. **Transformation:** transfer of naked DNA between cells of same species

2b. **Transduction through R plasmids:** R plasmids are a sexual transfer of plasmid DNA in a bacteria virus between bacteria of the same species

2c. **Conjugation:** the passage of gene from bacteria to bacteria via direct contact through a sex plus or bridge. Conjugation occurs primarily in GRAM NEGATIVE BACILLI. It is the principal mechanism of acquired resistant among enterobacteria

2d. **Transposition:** occurs as a result of movement or "jumping or transposons" (stretches of DNA containing insertion sequences at each end) from plasmid to plasmid or from plasmid to chromosome and back

Mechanisms of Antimicrobial Resistance

1. Reduced entry of antibiotic into pathogen
2. Enhanced export of antibiotic by pathogen efflux pumps
3. release of microbial enzymes that destroy the antibiotic
4. Alterations of microbial enzymes that are required to transform products to the effective moieties
4. Alterations of target proteins
5. Development of alternative biochemical pathways to those inhibited by the antibiotic

Factors that Promote Antimicrobial Resistance

1. Exposure to sub-optimal levels of antimicrobial
2. Exposure to microbes carrying resistance genes

Inappropriate Antimicrobial Use

- Prescriptions not taken correctly
- Antibiotics for viral infections (you don't give antibiotics for viral infections)
- Antibiotics sold without medical supervision
- Spread of resistant microbes in hospitals due to lack of hygiene
- Lack of quality control in manufacture of outdated antimicrobial
- Inadequate surveillance of defective susceptibility assays
- Poverty or way
- Use of antibiotics in foods

Antibiotics in Foods

Antibiotics are used in animal feeds and sprayed on plants to prevent infection and promote growth

Multi-drug resistant *Salmonella typhi* has been found in some people who eat beef fed antibiotics

MRSA "mer-sah"

Methicillin-Resistant Staphylococcus Aureus

Most frequent nosocomial (hospital-acquired) pathogen

Usually resistant to several other antibiotics



By heatherisawesome
(x0xheather_)

cheatography.com/x0xheather/

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