

### Antibiotics

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

Talking about chemical products 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  
Ethambutol  
Pyrazinamide  
Isoniazid

**DNA Synthesis & Integrity Inhibitors** Sulfonamides  
Trimethoprim  
Quinolones

**Transcription & Translation Inhibitors** Rifampin  
Aminoglycosides  
Spectinomycin  
Tetracyclines  
Macrolides  
Chloramphenicol  
Streptogramins  
Oxazolidinones



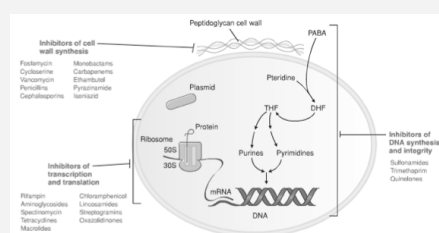
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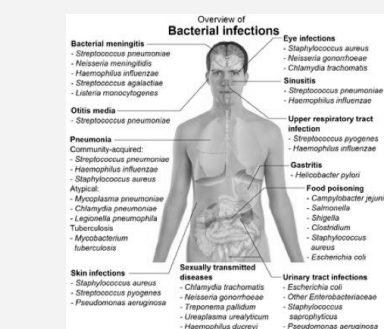
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### Site of Action of Antibacterial Drug Classes



### 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



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