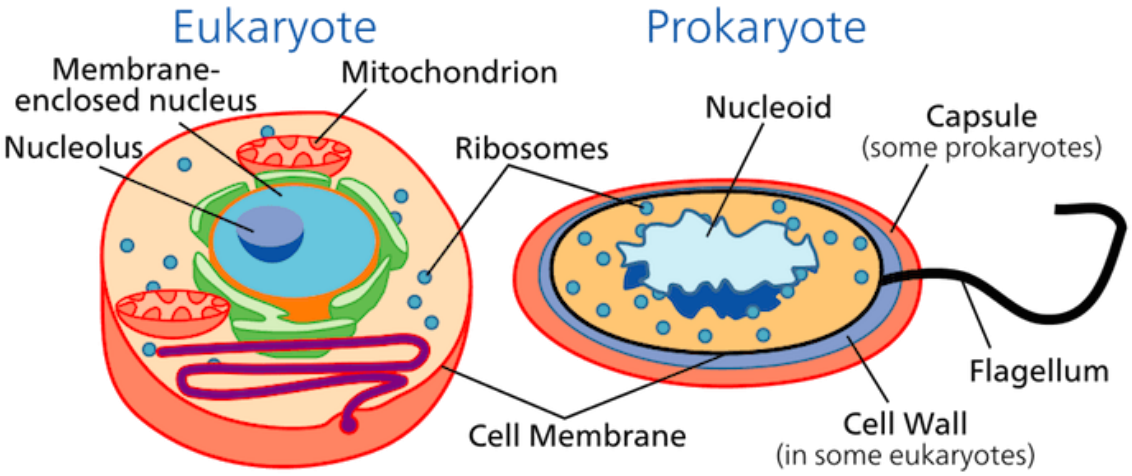
Principles of Antimicrobial Therapy

Antimicrobial therapy takes advantage of the biochemical differences that exist between microorganisms and human beings.

*they have the ability to injure or kill an invading microorganism without harming the cells of the host.

* Bact. DNA exposed and not protected by membrane.



Classification of antimicrobial agents

1. Source of antibiotic:

- **Natural**: penicillin, aminoglycosides

- **Synthetic**: Quinolone, sulfonamide

- **Semisynthetic:** ampicillin, amoxicillin

2. Mode of action:

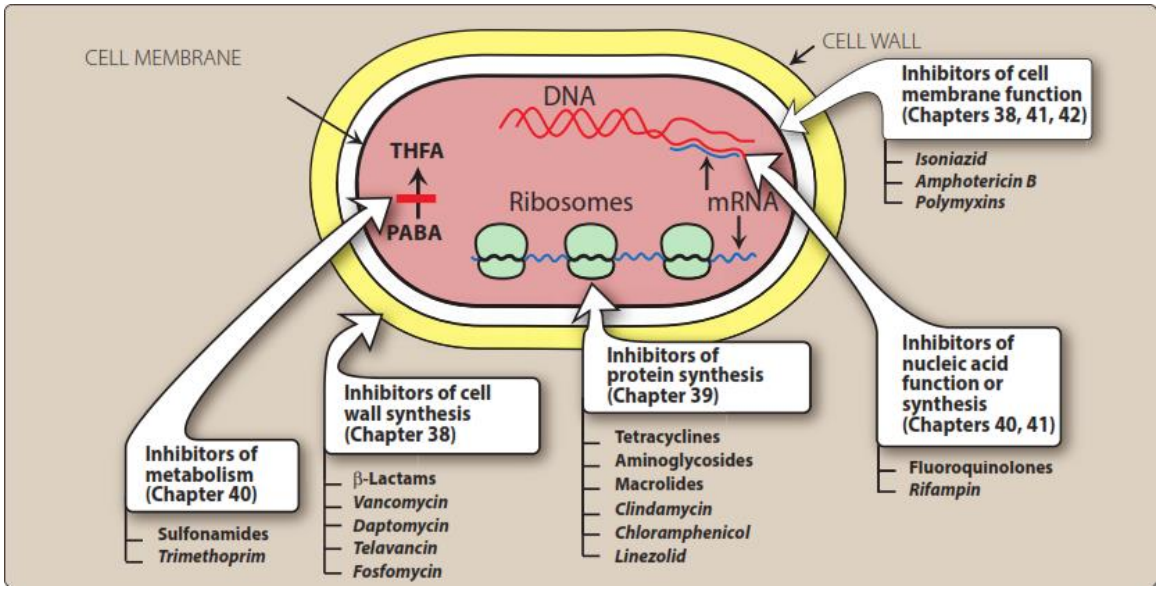
A- Bacteriostatic: arrest the growth and replication of bacteria at serum (or urine) levels achievable in the patient

B- Bactericidal: kill bacteria at drug serum levels achievable in the patient.

It is possible for an antibiotic to be bacteriostatic for one organism and bactericidal for another.

For example, linezolid is bacteriostatic against *Staphylococcus aureus* and *enterococci* but is bactericidal against most strains of *S. pneumoniae*.

3. Mechanism of action



Clinical approaches to antimicrobial prescription

1- Right patient

confirm the presence of infection (Fever, CBC, Special tests)

2. Right drug (selection of Antimicrobial Agent)

A- Identification of the infecting organism

- A rapid assessment of the nature of the pathogen can sometimes be made on the basis of the Gram stain
- it is necessary to culture the infective organism and determine the susceptibility
- obtain a sample culture of the organism prior to initiating treatment.
- Definitive identification may require other laboratory techniques, such as microbial antigens, DNA, or RNA, or an inflammatory or host immune response

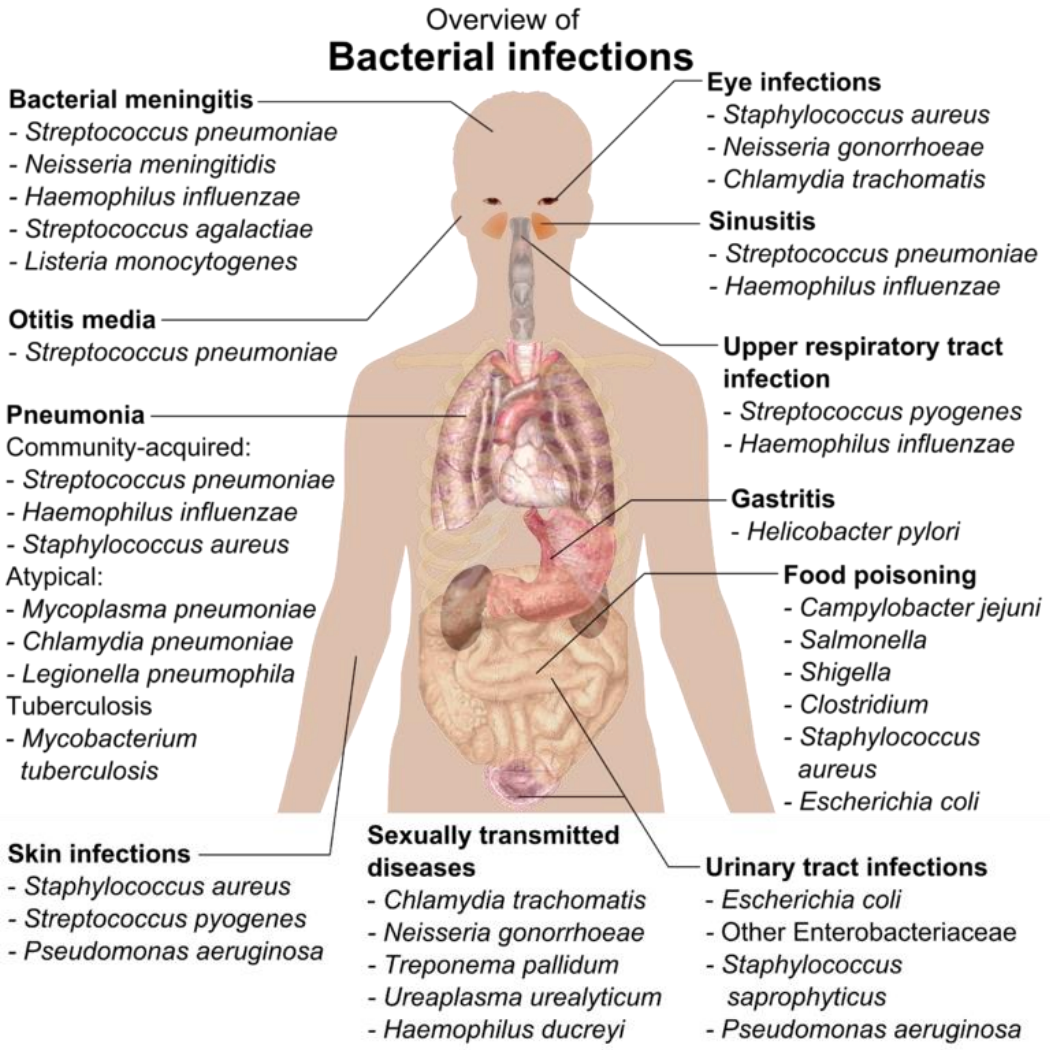
Empiric therapy

Timing:

Acutely ill patients (neutropenic patient, meningitis)

Selecting a drug

1. site of infection
2. the patient's history (for example, previous infections, age, recent travel history, recent antimicrobial therapy, immune status, and whether the infection was hospital- or community-acquired). (mening. & strep.)



B- Patient factors

Immune system:

- ❖ Alcoholism, diabetes, HIV infection, malnutrition, autoimmune diseases, pregnancy, or advanced age can affect a patient's immunocompetence, as can immunosuppressive drugs.
- ❖ High doses of bactericidal agents or longer courses of treatment may be required

Renal dysfunction:

- ❑ Poor kidney function may cause accumulation of certain antibiotics.

Hepatic dysfunction:

- ❑ Antibiotics that are concentrated or eliminated by the liver (for example, erythromycin and doxycycline) must be used with caution when treating patients with liver dysfunction.

Poor perfusion (tissue penetration):

- ❑ Chronic abscess
- ❑ Diabetic foot (ischemia)
- ❑ Natural barriers: (BBB, vitreous body (eye), prostate)

Age:

- ➢ neonate (chloramp. & sulfonam. Contra.)
- ➢ Child. : (tetracyc. & flouroquin. Conra.)
- ➢ Elderly : (aminogly.)

Pregnancy and lactation:

- ➢ (aminogly., flouroquin.)

Risk factors for multidrug-resistant organisms:

- prior antimicrobial therapy in the preceding 90 days
- hospitalization for greater than 2 days within the preceding 90 days
- current hospitalization exceeding 5 days
- high frequency of resistance in the community or local hospital unit
- Immunosuppressive diseases and/or therapies.

C. Safety of the agent

- Antibiotics such as the penicillins are among the least toxic of all drugs because they interfere with a site or function unique to the growth of microorganisms.
- chloramphenicol have less specificity and are reserved for life-threatening infections because of the potential for serious toxicity to the patient.

D. Cost of therapy

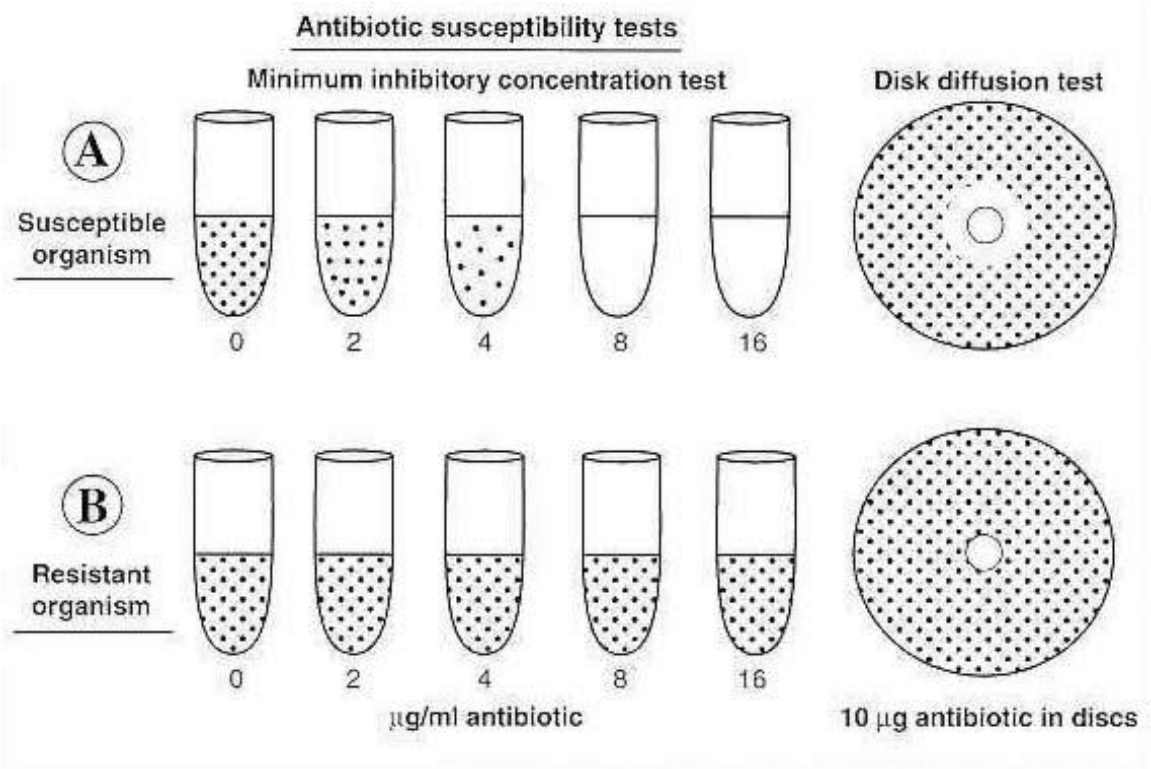
3. Right dose

Minimum inhibitory concentration (MIC):

- the lowest antimicrobial concentration that prevents visible growth of an organism after 24 hours of incubation.

Minimum bactericidal concentration (MBC):

- the lowest concentration of antimicrobial agent that results in a 99.9% decline in colony count after overnight broth dilution incubations



Concentration-dependent killing:

- gentamicin 40mg tid, then 80mg twice, then 160mg once daily

Time-dependent (concentration-independent) killing:

- β-lactams, glycopeptides, macrolides, clindamycin, and linezolid do not exhibit concentration-dependent killing

Postantibiotic effect:

- The PAE is a persistent suppression of microbial growth that occurs after levels of antibiotic have fallen below the MIC.
- for example, aminoglycosides and fluoroquinolones often require only one dose per day, particularly against gram negative bacteria.

4. Right rout

- depend on type and severity of infection

5. Right duration

All infections have international quid lines for ex:

Tonsillitis ------ 3-5 days

Uti ---------- 10 d

Pneumon. -------7 d

Meningitis ------ 15 d

Note: it preferred to continue with antibiotic about 2-3 days after complete cure to prevent infection relapse = resistance

CHEMOTHERAPEUTIC SPECTRA

Narrow-spectrum antibiotics

- acting only on a single or a limited group of microorganisms.
- For example, isoniazid is active only against Mycobacterium tuberculosis

Extended-spectrum antibiotics

- modified to be effective against gram-positive organisms and also against a significant number of gram-negative bacteria. For example, ampicillin.

Broad-spectrum antibiotics

- affect a wide variety of microbial species (tetracycline, fluoroquinolones and carbapenems)

Antimicrobial combination

Combination in the following:

- Mixed infection (diabetic foot & peritonitis)
- Sever inf. (meningitis)
- Highly resistant bact. (TB, pseudomon.)

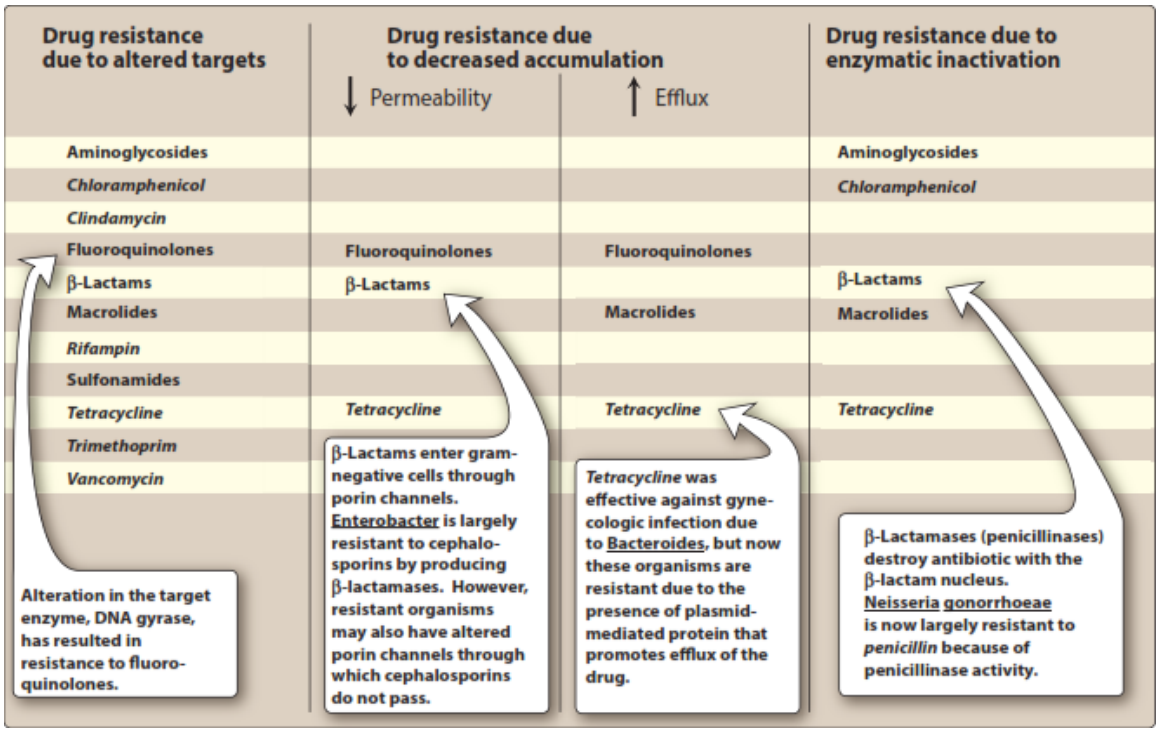
- Synergism (sulfa & trimeth., penicill. +ve & aminogl. -ve)

Cidal + cidal = very good (synergism)

Static + static = addition (tetra + erythr)

Cidal + static = unknown, often bad (penicill. + tetrac.)

DRUG RESISTANCE



PROPHYLACTIC USE OF ANTIBIOTICS

Certain clinical situations, such as **dental procedures** and **surgeries**, require the use of antibiotics for the **prevention** rather than for the **treatment** of infections.

COMPLICATIONS OF ANTIBIOTIC THERAPY

A. Hypersensitivity

the **penicillins**, despite their almost absolute selective microbial toxicity, can cause serious **hypersensitivity** problems, ranging from **urticaria** (hives) to **anaphylactic shock**.

B. Direct toxicity

Aminoglycosides can cause **ototoxicity** by interfering with membrane function in the auditory hair cells.

C. Superinfections

Drug therapy, particularly with **broad-spectrum** antimicrobials or **combinations** of agents, can lead to alterations of the **normal microbial flora** of the upper respiratory, oral, intestinal, and genitourinary tracts, permitting the overgrowth of opportunistic organisms, especially fungi or resistant bacteria.