# Anti-microbial Therapy

Pharmacology 3

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**Chemotherapy**: is the use of chemical agents (either synthetic or natural) to destroy infective agents (microorganisms' i.e bacteria, fungus and viruses, protozoa, and helminthes) and to  inhibit the growth of malignant or cancerous cells

**Antimicrobials**: are chemical agents (synthetic/natural) used to treat bacterial, fungal and viral infections. Antibiotics: are substances produced by various species of microorganisms (bacteria,fungi, actinomycetes) that suppress the growth of other microorganisms. Antimicrobial drug exhibits selective toxicity. I.e. the drug is harmful to the parasite without being harmful to the host.

When derived from living organism, they are termed **antibiotics**

- ❖ The most imp thing that these drugs should do no harm to the host cell.

- ❖ (Highly selectivity drugs against M.O rather than human cells)
- ❖ From where did this selectivity of these drugs come????

- The ability to injure or kill an invading microorganism without harming the cells of the host.
- The biochemical differences that exist between microorganisms and human beings.

# Classification of antimicrobial agents

1. According to the **CAUSTIVE AGENTS (The type of organism) against which they are active.**

(bacteria, virus, fungi) `either (antibacterial, antiviral, antifungal & so on)

2. According to their structure (Macrolides, Aminoglycosides, Tetracyclines)

# 3. According to their mechanism of action

**Inhibition of cell wall synthesis**

- Penicilin , cephalosporin , bacitracin , vancomycin

**Inhibition of functions of celluler membrane**

- Polymyxins

**Inhibition of protien synthesis**

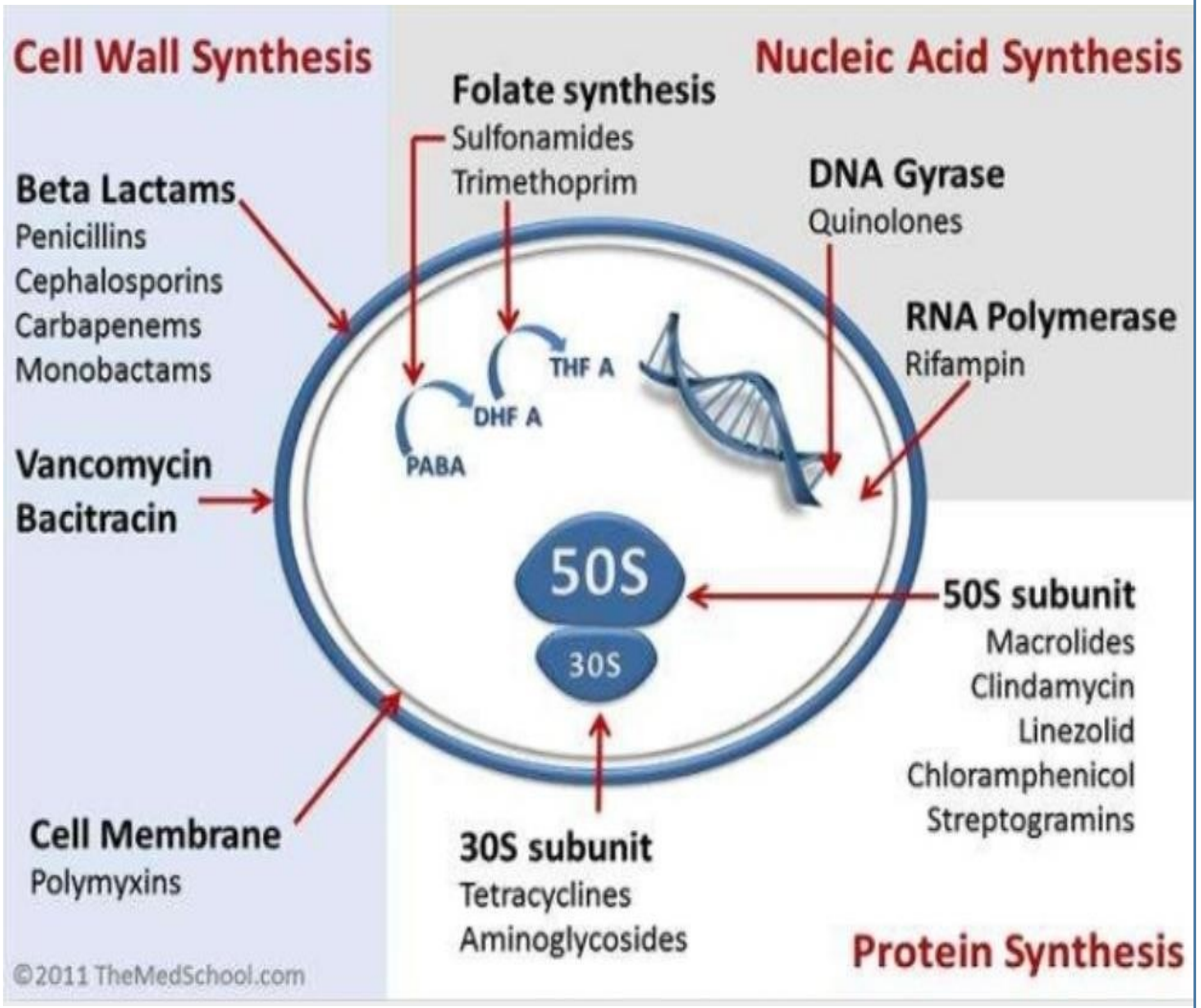
- Chloramphenicol , clindamycin & macrolides
- Tetracyclines & aminoglycosides

**Inhibition of nucleic acid synthesis**

- Quinolones
- Rifampin

**Inhibition of folic acid synthesis**

- Sulfonamides & trimethoprim



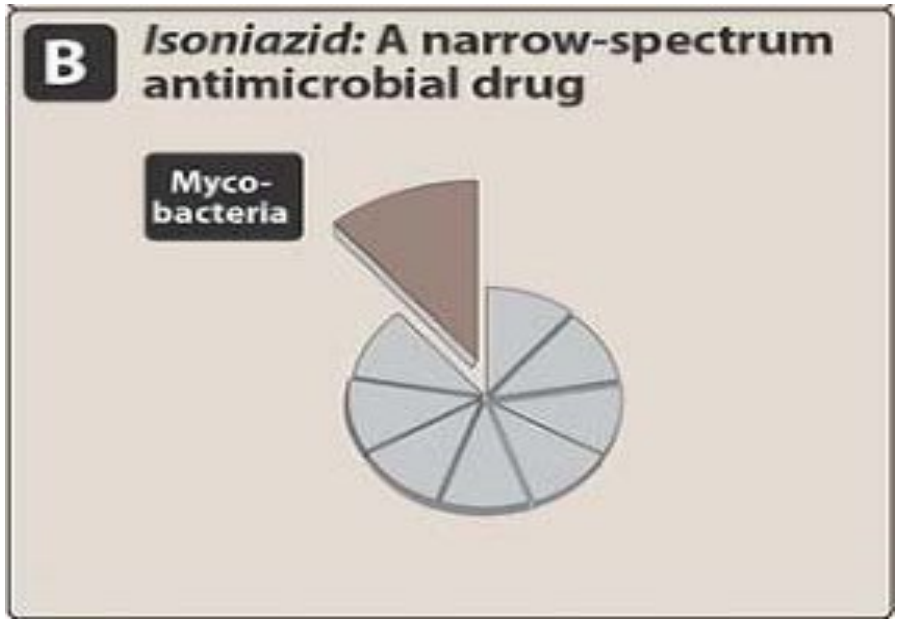
## 4- According to the Spectrum of activity

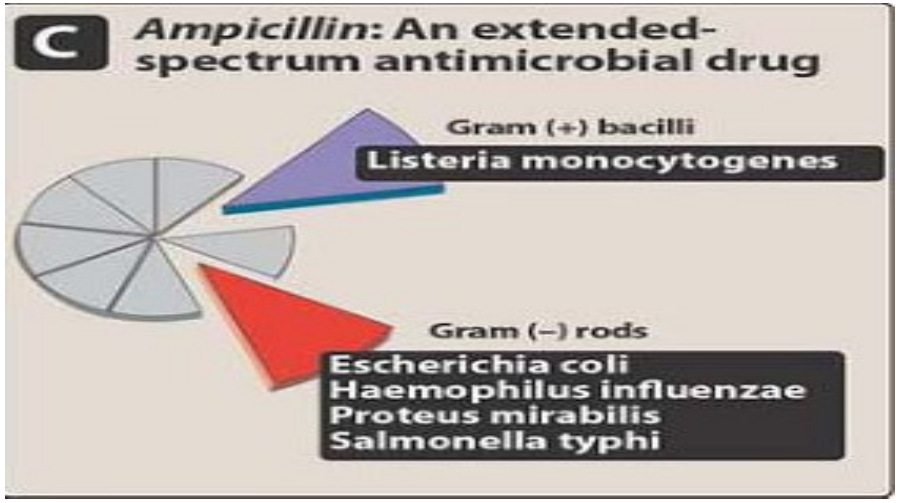
Spectrum: the range of microorganisms that a drug is effective against.

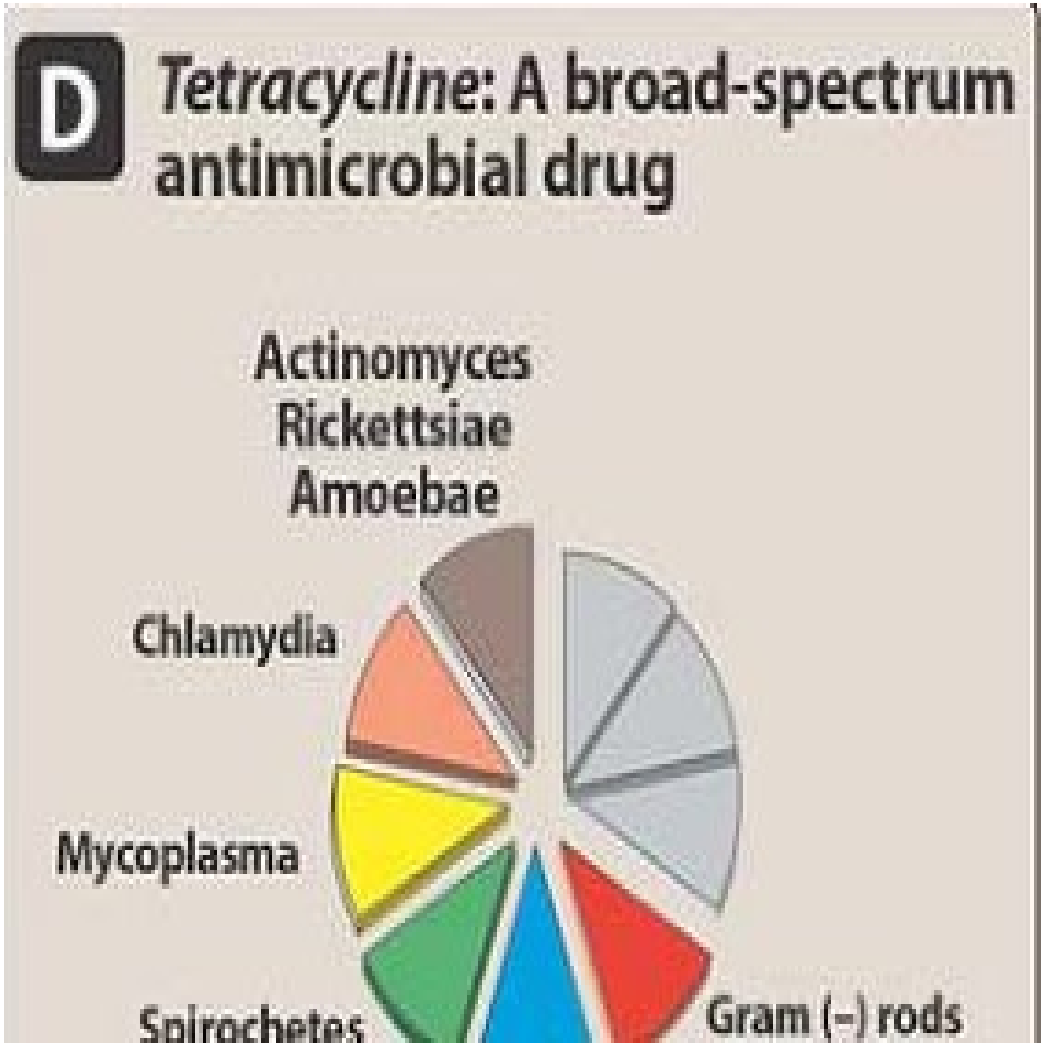
1. **Narrow spectrum** antibiotic: active against single or limited group of M.O. (Isoniazid)

2. **Extended spectrum :** is one that, as a result of chemical modification, affects additional types of bacteria, usually those that are gram-negative. active against types of bacteria G- & G+.
( Ampicillin)

3. **Broad spectrum:** active against a wide variety of microbial species.
(Tetracyclines, quinolones, Chloramphenicol).


B
Isoniazid: A narrow-spectrum antimicrobial drug
Myco-bacteria


C
Ampicillin: An extended-spectrum antimicrobial drug
Gram (+) bacilli
Listeria monocytogenes
Gram (–) rods
Escherichia coli
Haemophilus influenzae
Proteus mirabilis
Salmonella typhi


D
Tetracycline: A broad-spectrum antimicrobial drug
Actinomyces
Rickettsiae
Amoebae
Chlamydia
Mycoplasma
Spirochetes
Gram (–) rods

# 5. By their action

## 1. Bacteriostatic drugs

They **arrest/inhibit** (**stops does not kill it)** the growth & replication of the bacteria.

**Given to pts who have good immunity.**

**E.x.**

Sulphonamides,

Trimethoprim, Tetracyclines, macrolides, Clindamycin, Chloramphenicol.

## 2. Bactericidal drugs

**-kills** the bacteria that are rapidly dividing or multiplying.

-more preferable in pts who have low immunity. (HIV patients, cancer patients, taking steroids)

**E.x.**

Vancomycin ,B-lactams, Aminoglycosides, Rifampicin

Sometimes (not a rule) when you combine two of these bacteriostatic in one drugs, the new drugwill become bactericidal.

**EXAMPLES:**
Chloramphenicol
Erythromycin
Clindamycin
Sulfonamides
Trimethoprim
Tetracyclines


**EXAMPLES:**
Aminoglycosides
Beta-lactams
Vancomycin
Quinolones
Rifampin
Metronidazole

# Selection of Antimicrobial Agents

## 1- Making the diagnosis :

- ✓ To be sure that the patient is suffering from an bacterial infection.
- ✓ Know the site of infection( GI,RT,UT).
- ✓ Take the required specimen from the patient.(blood , CSF, mid stream urine ,ear swap, vaginal discharge)
- ✓ Identify the organism.

## 2-Remove the pathological barrier to cure

**(abscess ,obstruction).**

**3-Select the best drug :**So that it reach site of infection in the therapeutic conc.

- ➢ Drug properties: PK,TI.
- ➢ **Optimum dose & frequency**
- ➢ **the most appropriate route of administration**

## 4- The cost of therapy.

## 5-Patient factors:

1. Immune system.
2. Renal dysfunction.
3. Hepatic dysfunction.
4. Poor perfusion.
5. Age.
6. Pregnancy.
7. Lactation.
8. Concomitant medication.
9. Allergy.

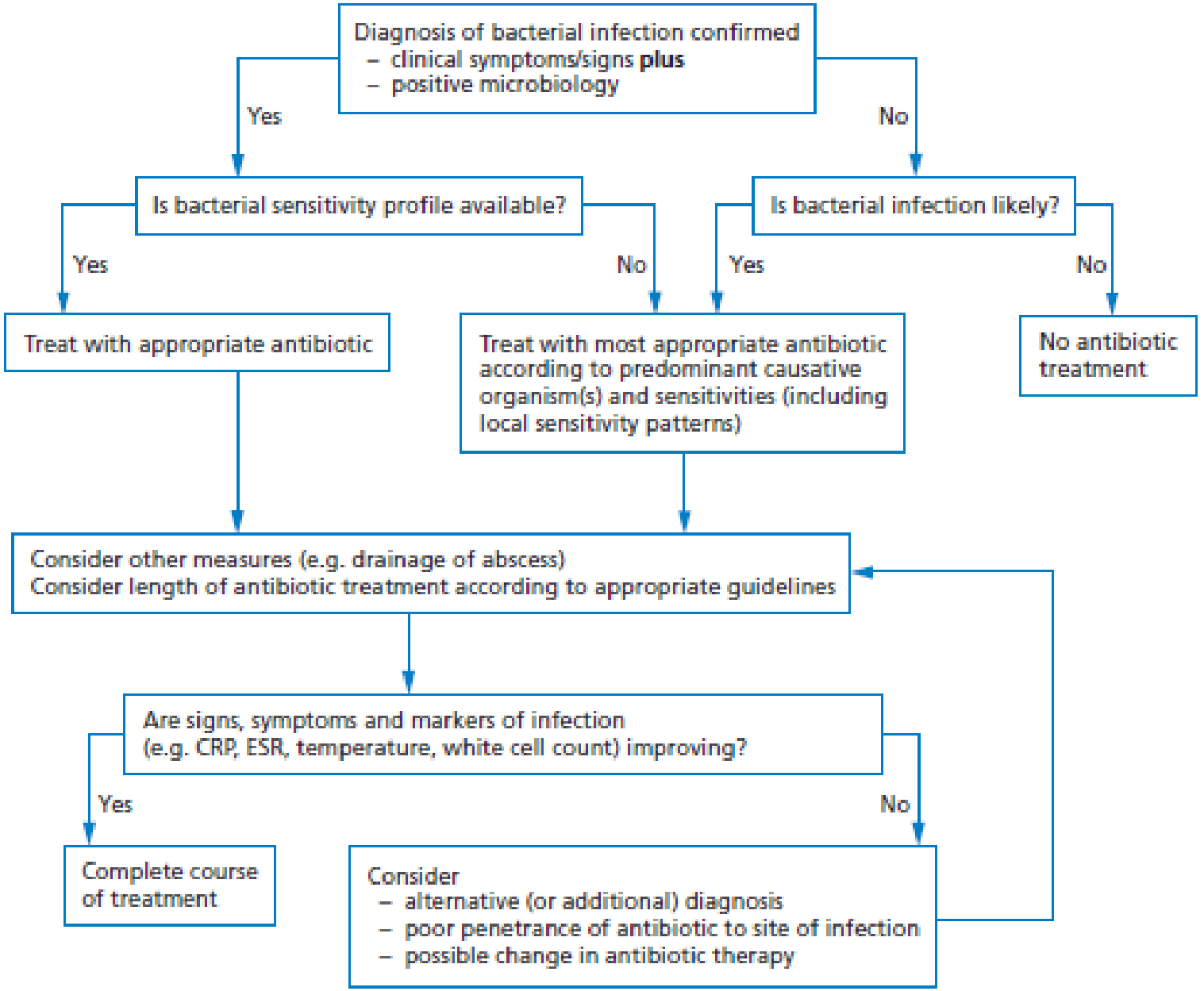



Figure 43.1: General algorithm for the treatment of bacterial infections.

- *Ideally*, the antimicrobial agent used to treat an infection is selected *after* the organism has been identified and its drug susceptibility established.

- However, in the critically ill patient, such a delay could prove fatal, and immediate *empiric* therapy is indicated.

- **Empiric therapy:** is treating the patient without knowing the causative organisms & their sensitivity test.
- Immediate administration of the drug prior to identification of bacteria and sensitivity test.(or the specimens is obtained but lab result not available)

- **Definitive therapy :**

treating exactly the causative agent depending on its sensitivity test (done after receiving the results of test)

- **Prophylactic therapy:**

Used drugs to prevent an infection rather than to treat , to maintain health and prevent the spread of disease.

# Prophylactic antibiotics

1. To prevention of opportunistic infection
   - ❖ In bowel surgery to prevent peritonitis
   - ❖ In dental manipulation to prevent bacterial endocarditis in patients with abnormal heart valves.

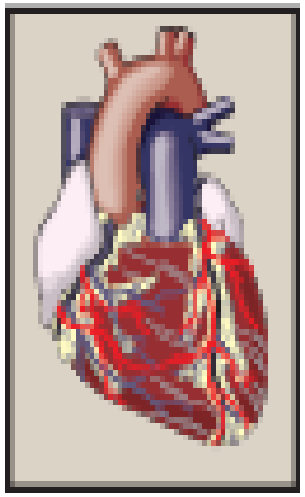
2. Prevention of spread among contacts.

.

- ❖ Rifampicin to prevent Meningitis.
- ❖ Chloroquine to prevent Malaria.

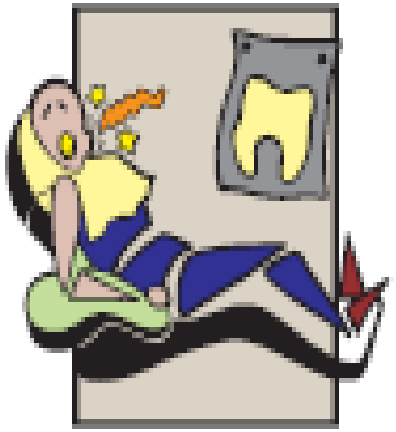
## 1

Pretreatment may prevent streptococcal infections in patients with a history of rheumatic heart disease. Patients may require years of treatment.



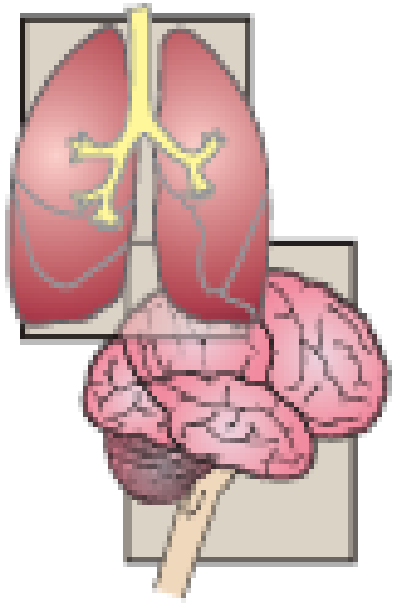
## 2

Pretreating of patients undergoing dental extractions who have implanted prosthetic devices, such as artificial heart valves, prevents seeding of the prosthesis.



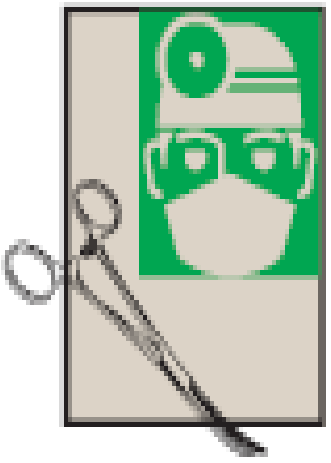
## 3

Pretreatment may prevent tuberculosis or meningitis among individuals who are in close contact with infected patients.



## 4

Treatment prior to most surgical procedures can decrease the incidence of infection afterwards. Effective prophylaxis is directed against the most likely organism, not



## 3- To prevent infection or disease :

- To prevent recurrent **UTI: Co-Trimoxazole** twice per week

- to prevent **Rheumatic fever :** young man who is having recurrent **tonsillitis**, we start giving him a monthly interval long acting **Benzathine penicillin** to prevent the acute streptococcal infection from coming back.

# Advantages of drugs combination

1. To delay or avoid the development of resistance.
   (Ex. Tuberculosis)
2. To broaden the spectrum of activity. (Mixed infection , severe unknown infection,).
3. To obtain potentiation (synergistic effect).

   Ex: -B-lactams and aminoglycosides in endocarditis. Penicillin + Aminoglycosides

2 separate IV bolus injection ,with time interval to avoid interaction.

- Co-trimoxazole.

# Disadvantages of drugs combination

1. Concomitant administration of a second agent is usually bacteriostatic and may interfere with the action of the first drug that is bactericidal

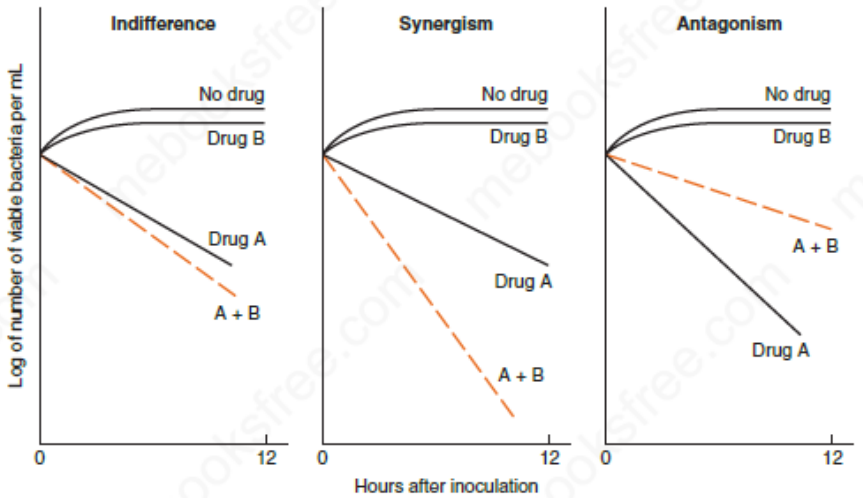
2. Suppression of normal flora, so give higher chance for opportunistic infection (**superinfection**).
3. Increased incidence of adverse reactions.
4. Highly cost

# Antibiotics Combination

**Synergistic:** Effects of the two agents in combination together multiply their therapeutic effect or one agent enhances the action of another normally inactive against the target organism (for example, aminoglycosides with a penicillins

- **Additive:** Effects of the two agents summate (for example, ciprofloxacin and metronidazole to treat aerobic and anaerobic gut flora).

- **Antagonistic:** Two agents interfere with each other (for example, tetracyclines and penicillin cannot be administered concurrently because of their chelation to one another).



# Problems with antimicrobial agents

1. Drug resistance. (the major problem )

(if the maximal level of that antibiotic that can be tolerated by the host does not halt bacterial growth).

- Limitation of drug resistance:

    1. Ensure that the indication, dose, duration are appropriate.
    2. Restrict use of drug combination to appropriate situations(TB).

2. Drug-drug interaction
3. Adverse effects.

## 3. Adverse effects

a. Hypersensitivity; (not dose related)

**e.g. Penicillin, cephalosporin.**

b. Toxic effect (dose related)

High serum levels of certain antibiotics may cause Direct toxicity / Organ toxicity

e.g. Aminoglycosides (ototoxicity)

- Chloramphenicol (Aplastic anemia)

**c. Superinfections: (clostridium difficile-colitis)**

alterations of the growth of normal flora of intestine, genitourinary tracts. Respiratory tract

Appearance of **a new infection** while treating an original infection (multiply C.difficile).

# How Effective is an Antibiotic

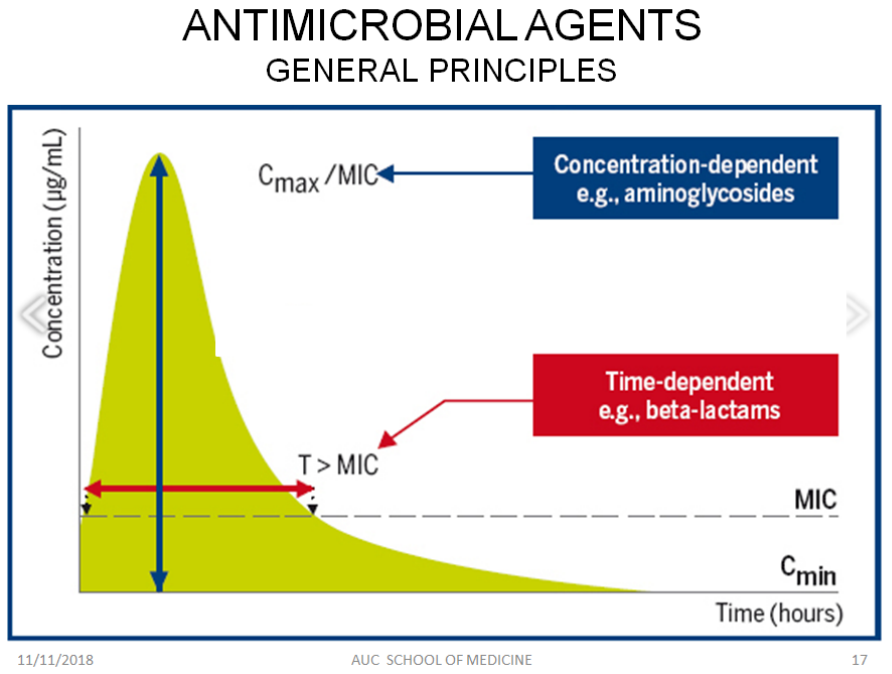
## Concentration Dependent Killing

Efficacy determined by magnitude of serum concentration above MIC
e.g. Aminoglycosides, quinolones.

## Time Dependent Killing

Efficacy determined by duration of time that serum concentrations exceed MIC

e.g. b-lactams, macrolides, cotrimoxazole

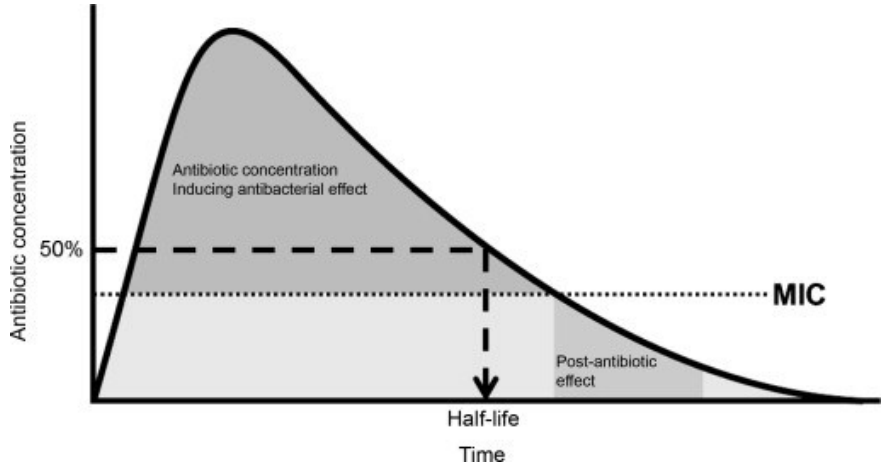


# How Effective is an Antibiotic

- **Post-antibiotic effect (PAE):**

phenomenon of continued bacterial killing even though serum concentrations have fallen below the minimum inhibitory concentration (MIC).

- Examples: **Aminoglycosides** and **Fluoroquinolones**.



# The End