

# Anti-microbial Therapy

Pharmacology 3  
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microbial chemotherapy      Cancer chemotherapy  
لكن المصطلح معروف أكثر للـ cancer

**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

لـ كل microorganisms

**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

بـ target موجود بالبكتيريا إـ شيء موجود بالبكتيريا مش موجود  
بالـ eukaryotic cells فيعملون targeting وصلك بمصلو selective  
toxicity يعني أنك الـ compound يكون toxic على البكتيريا  
رما يكون toxic على خلايا الإنسان (eukaryotic cells) مش  
مش دأخا بقه روا يعقوها شـ 100% بالتالي يكون ضرر  
على خلايا الإنسان.



- ❖ 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)

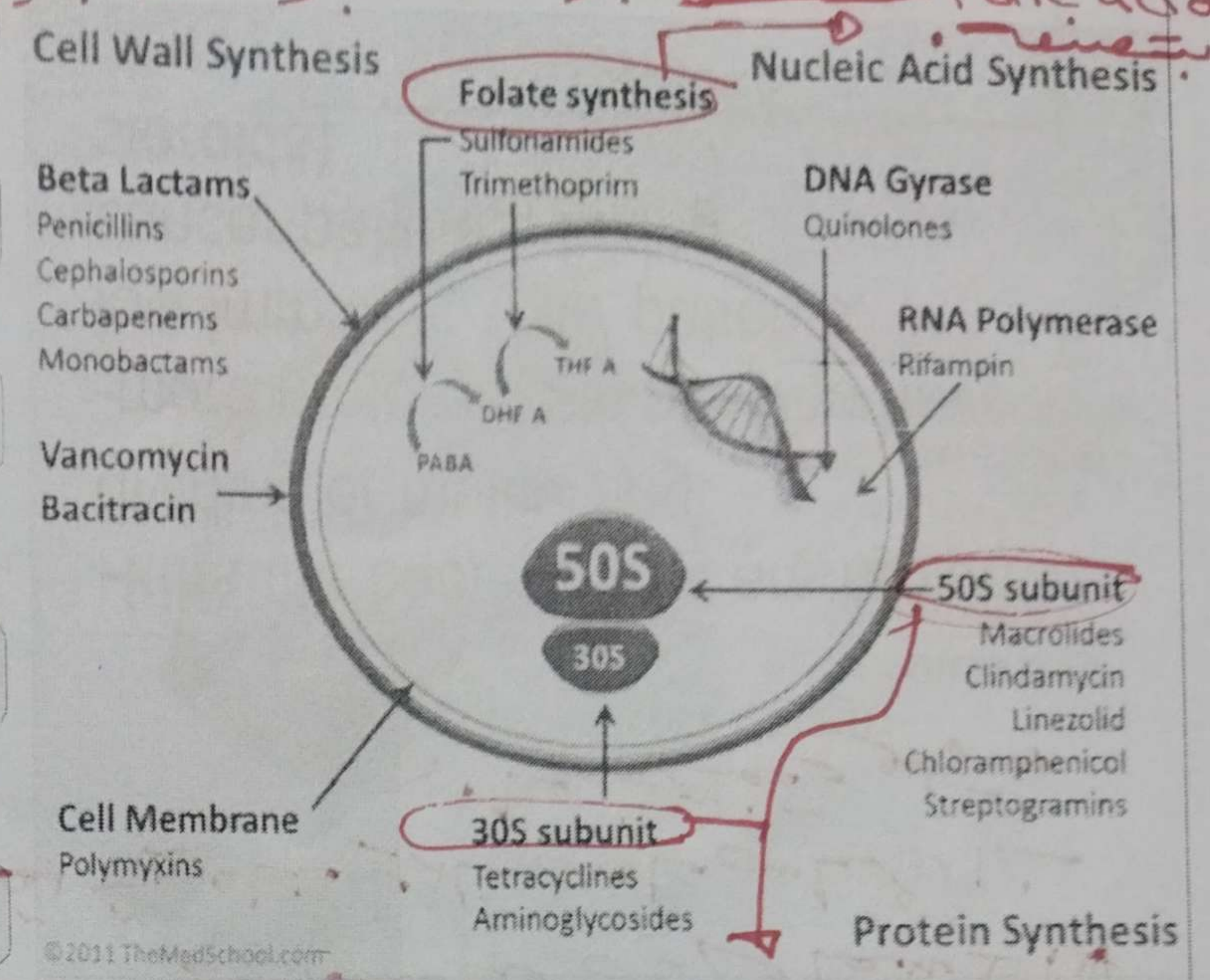


مسار MoA

### 3. According to their mechanism of action

العكاريات ما يتصف ببنوعه من برا كثر البكتريا  
Folic acid  
Nucleic Acid Synthesis

- Inhibition of cell wall synthesis**
  - Penicilin , cephalosporin , bacitracin , vancomycin
- Inhibition of functions of cellular 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



الرايبوسوم بالبكتريا مختلف عن الرايبوسوم  
بالعكاريات هذا هدف target

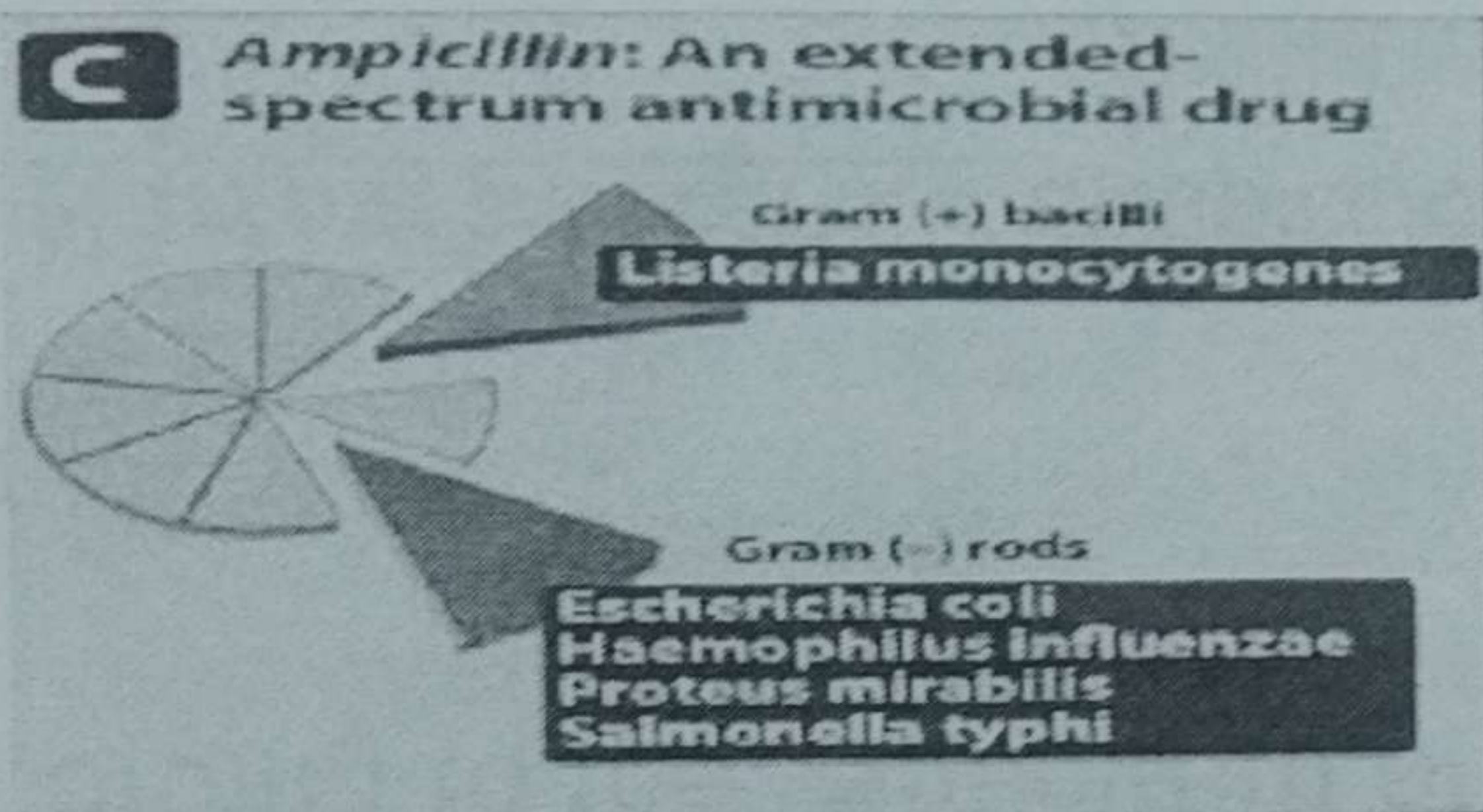
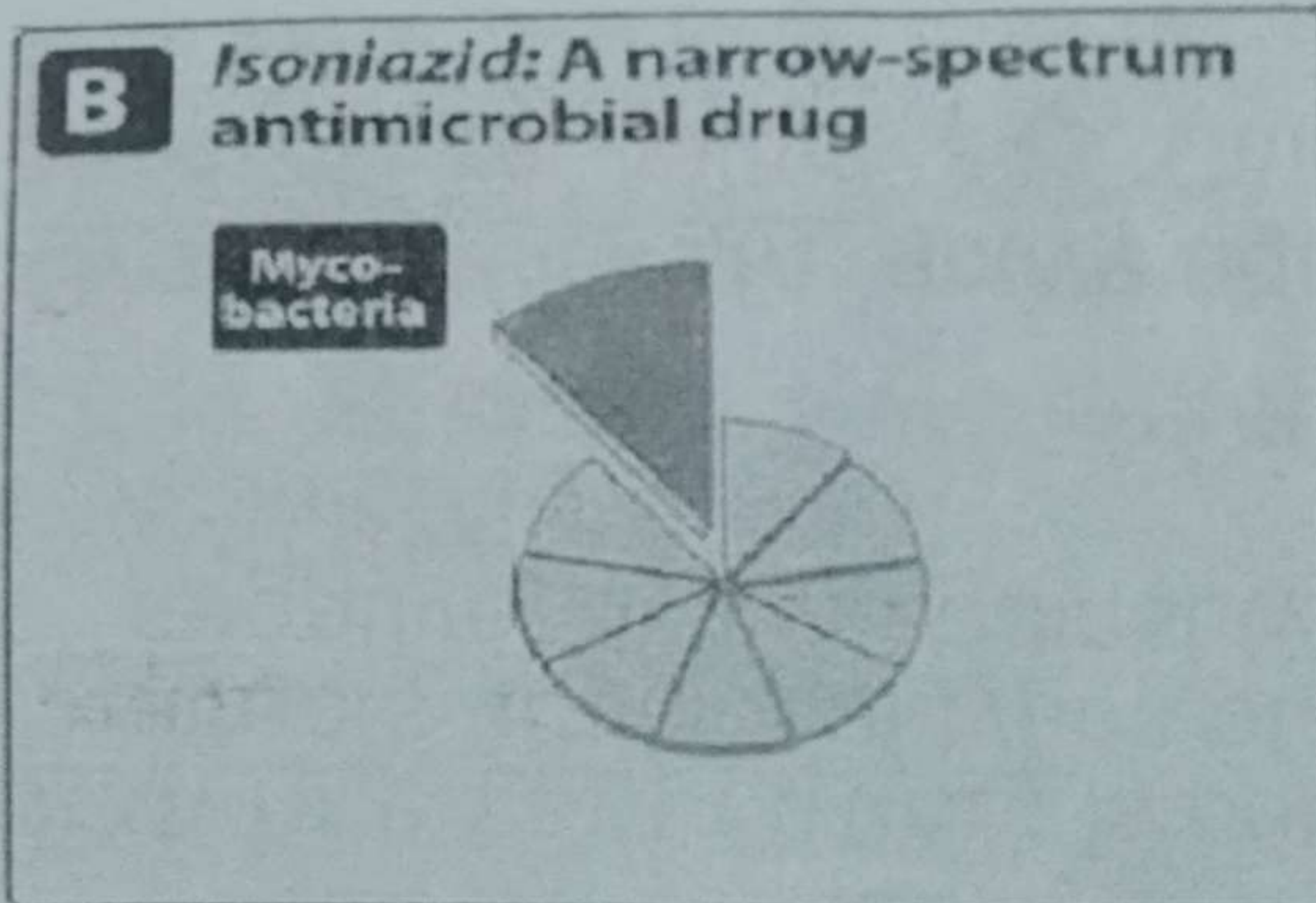
### 4. According to the Spectrum of activity

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

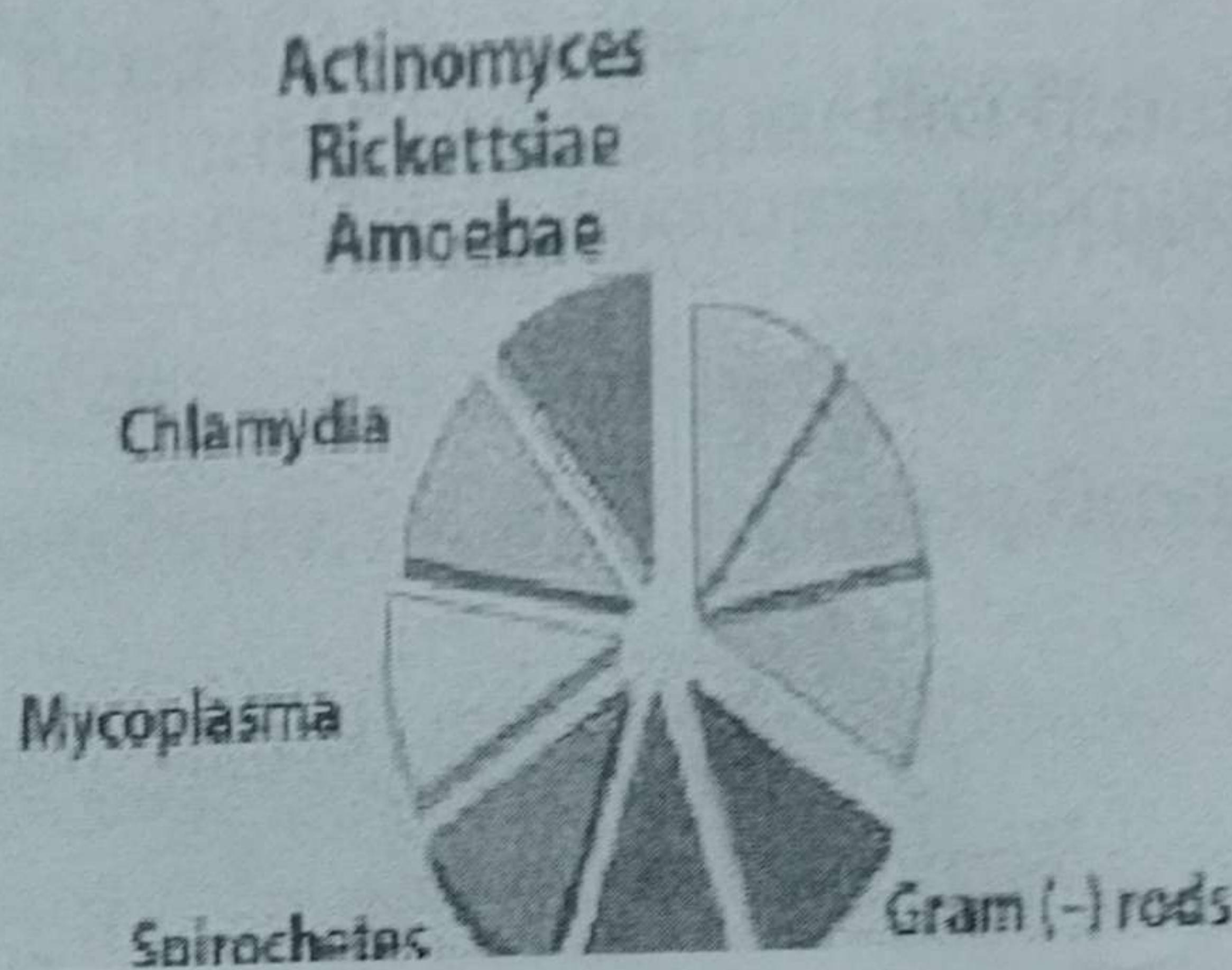
- Narrow spectrum** antibiotic: active against single or limited group of M.O. (Isoniazid)
- Extended spectrum** : is one that, as a result of chemical modification, affects additional types of bacteria, usually those that are gram-negative. active against types of bacteria G- & G+. (Ampicillin)
- Broad spectrum**: active against a wide variety of microbial species. (Tetracyclines, quinolones, Chloramphenicol).

مع أنه spectrum إلى أنه ينتظم narrow spectrum وهذا  
بسبب ال resistance لأنه بال broad يكون احتمال ال resistance  
أكثر إضافة أنه كلما كان broad أكثر فزع يعمل killing لا normal flora  
مخترية ال risk لل superinfection لأنه ال NF بطلية موجودة بال GI.





**D** Tetracycline: A broad-spectrum antimicrobial drug



\* إذا كانت صناعة الجسم طبيعية يمكن يوقف antibiotic أو مأيوضه لأنه  
جسمه يقاوم بجل Killing لا MO ومن تلقاء نفسه يتقاوم به فترة  
لكن لما بدأ أعطى antibiotic جعله bacteriostatic على شأن يوقف growth  
فالتالي يتنفس على عملية killing في جسمه بجسمه بكل طبيعته عنده بالأصل

\* الأسطفا في هذا فناعتهم قليلة المفروض نعطيه بacteria لأنها  
5. By their action من الأساس مامني خلايا مناعية تقاوم البكتيريا

### 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.

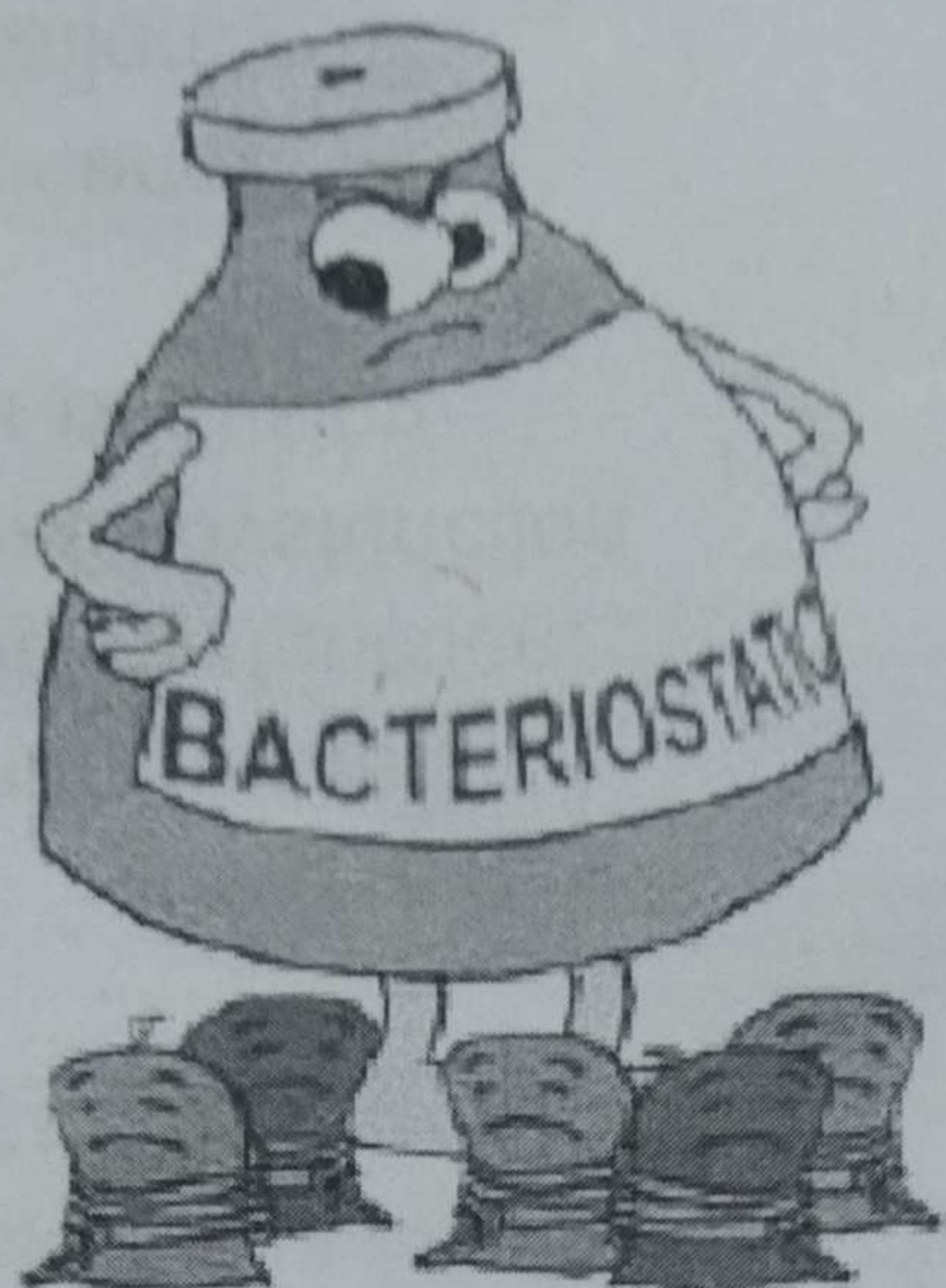
Vancomycin, B-lactams,  
Aminoglycosides, Rifampicin



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

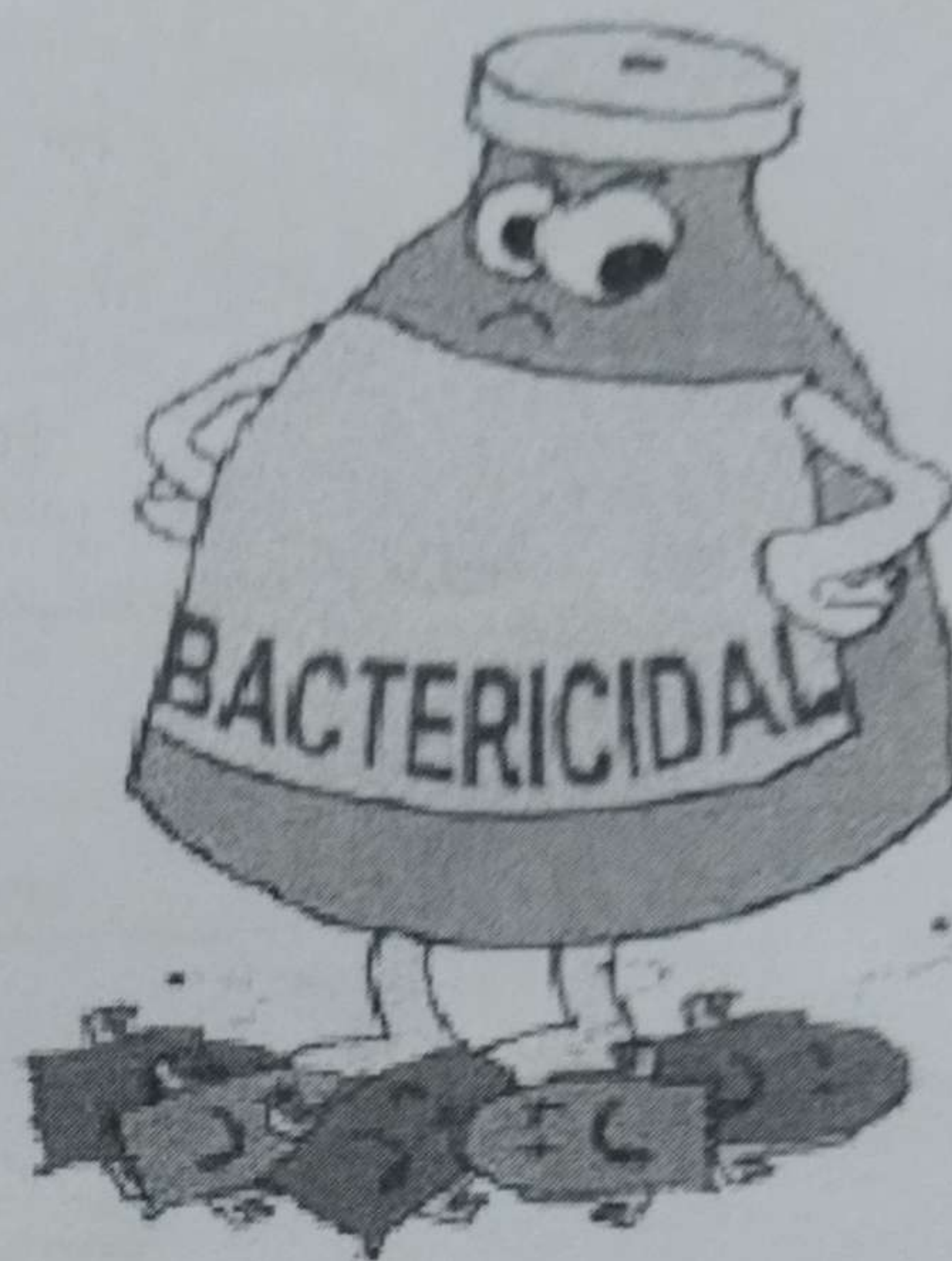
**EXAMPLES:**

Chloramphenicol  
Erythromycin  
Clindamycin  
Sulfonamides  
Trimethoprim  
Tetracyclines

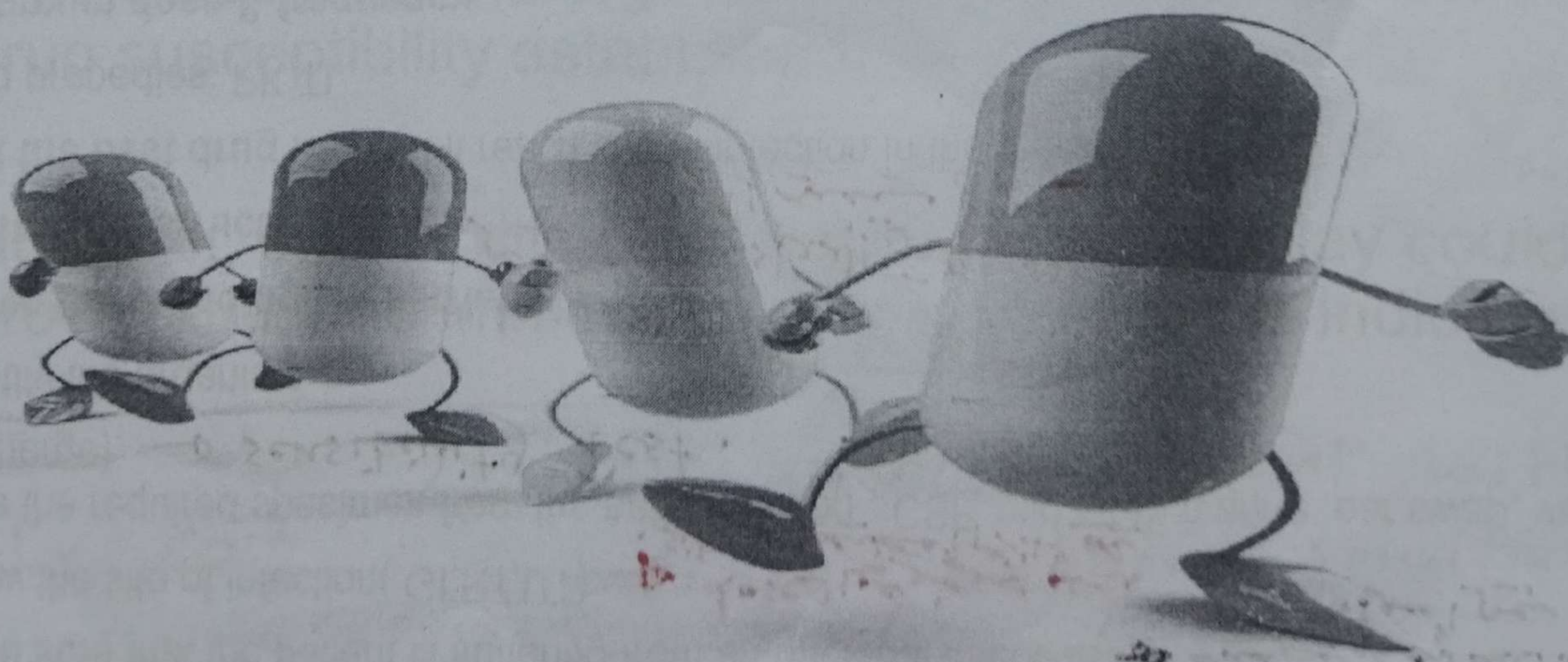


**EXAMPLES:**

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. → *مستلزم لو أعلية antibacti. الحريف عذو*
- ✓ Know the site of infection( GI,RT,UT). → *ممنوع منوع على dose*  
*هو لازم أعطيه الكمية*
- ✓ Take the required specimen from the patient.(blood , CSF, mid stream urine ,ear swap, vaginal discharge) → *sensitivity test.*
- ✓ 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.



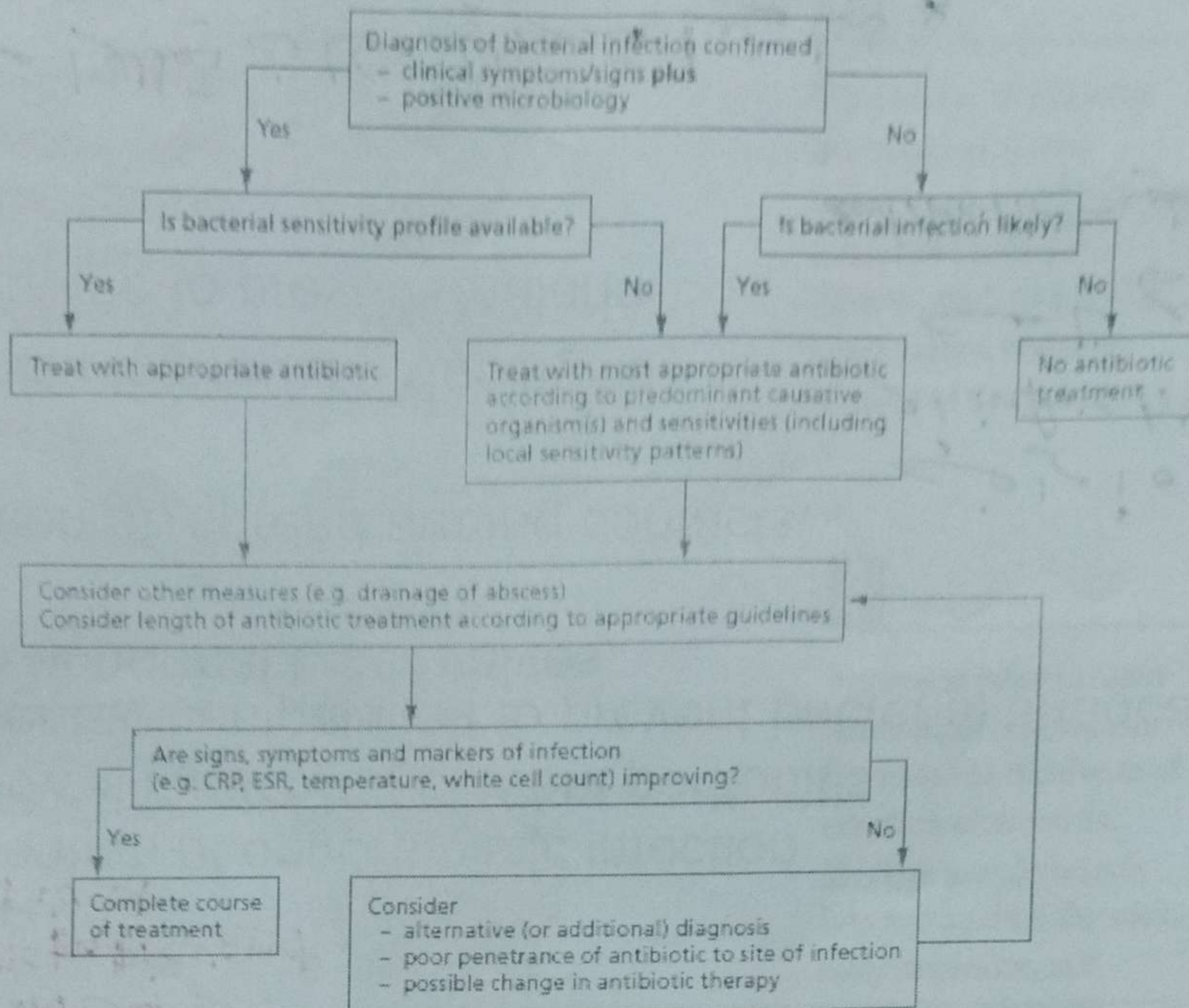


Figure 43.1: General algorithm for the treatment of bacterial infections.

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

*serious infection*

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

لأنه ما يقدر  
أن يتغير  
الحالات

↳ treating the patient with antibiotics before sensitivity test.



- ❑ 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.

• وقاية من العدوى

• Prevention of infection  
antibiotic to prevent infection

## 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.

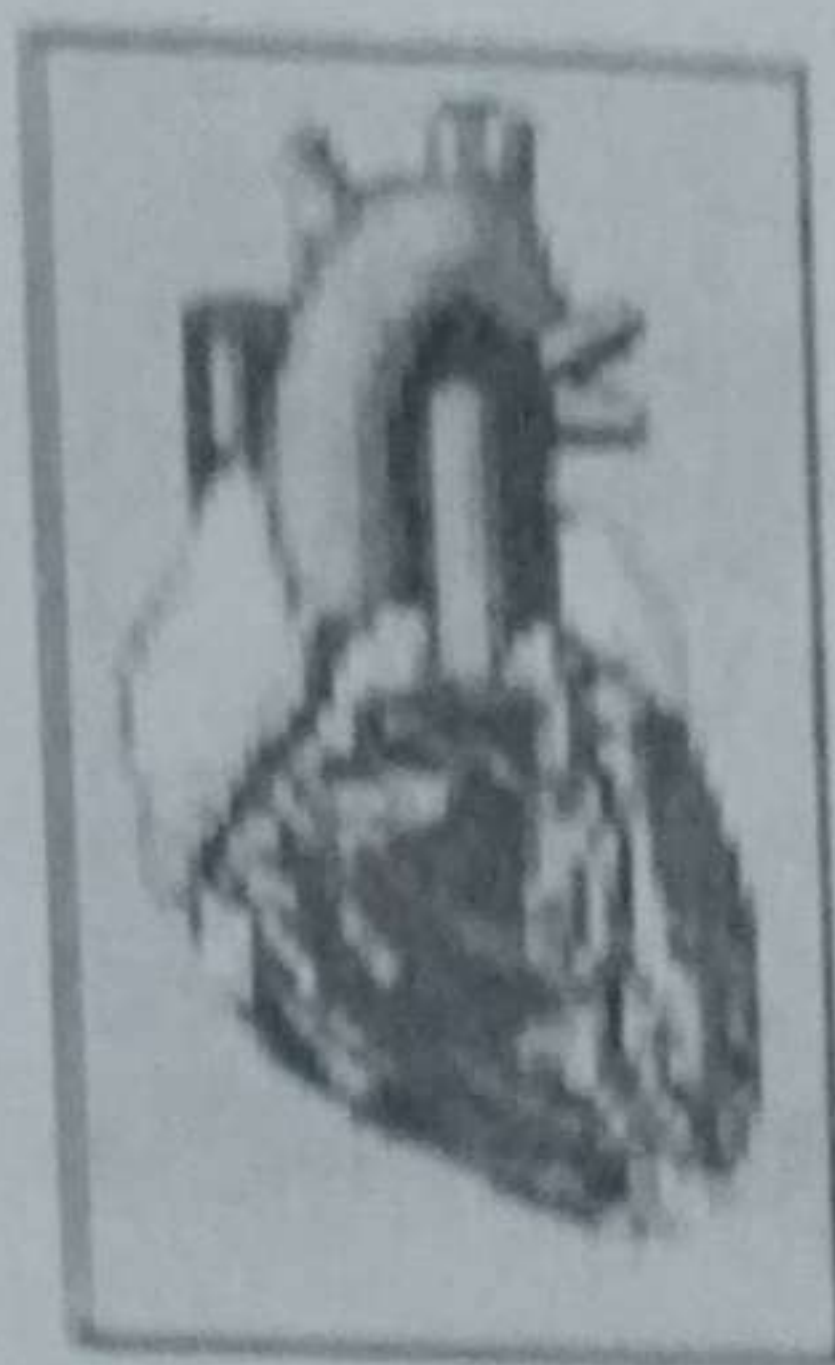
• مثلاً "صيف" عنه أمراض  
• بترتبه risk infection او  
• صيف في خط مع تاس  
• antibiotic في مريض infected

• يجب اولوا قدر الامكان يقللوا من  
• استخدام prophylactic therapy  
• على شان موصوفى resistance



**1**

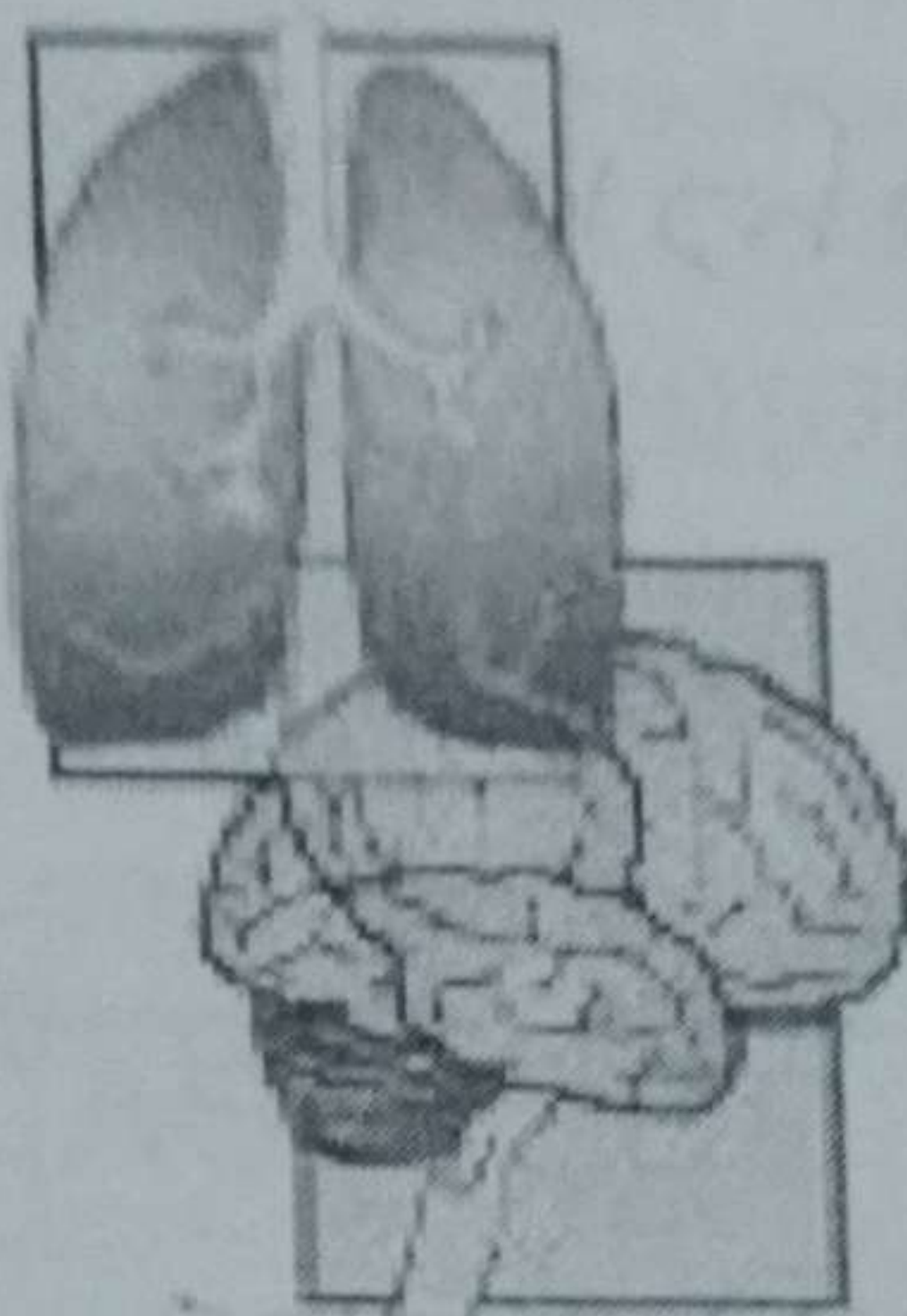
Pretreatment may prevent streptococcal infections in patients with a history of rheumatic heart disease. Patients may require years of treatment.

**2**

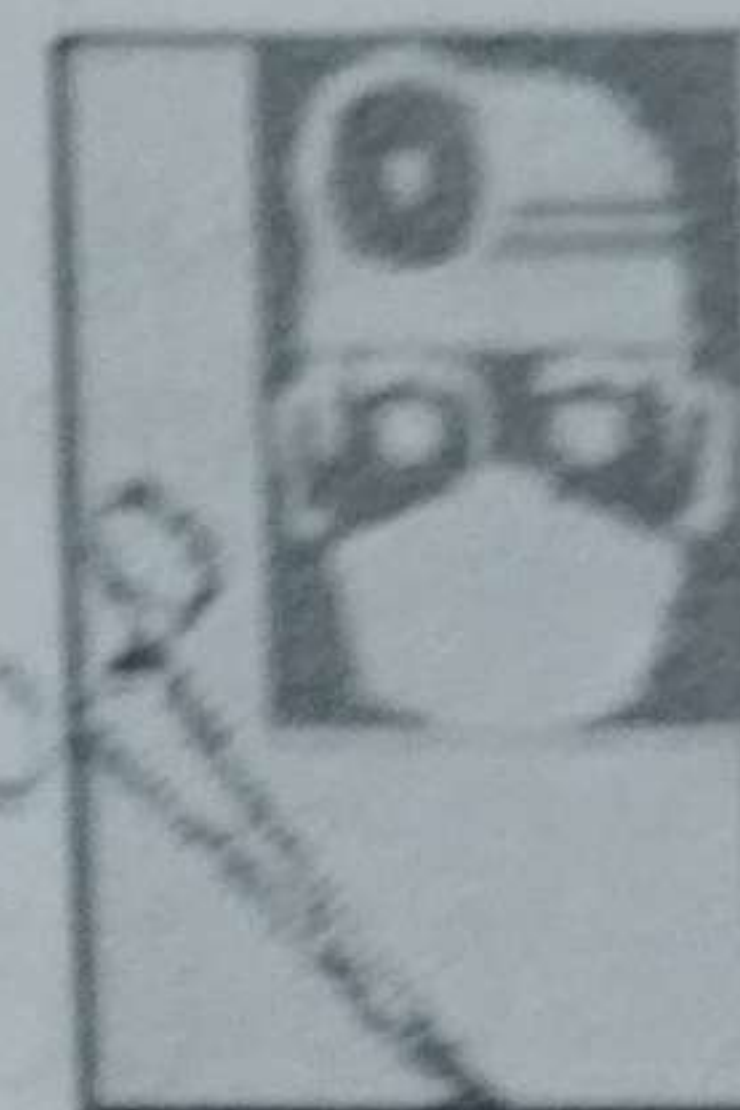
Pretreating of patients undergoing dental extractions who have implanted prosthetic devices, such as artificial heart valves, prevents seeding of the prosthesis.

**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 eradication of all flora.



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.



\* الممزوجة والأفضل ما التجميد combination إذا بقدر لكن بالحالات المذكورة لا تزم التجميد combination.

### Advantages of drugs combination

1. To delay or avoid the development of resistance. (Ex. Tuberculosis)   
 البكتيريا بتعمل tuberculosis إذا عالها بـ antibiotic واحد على طول بتعمل resistance.
2. To broaden the spectrum of activity. (Mixed infection, severe unknown infection,)   
 على شئنا نغطوا على أنوع البكتيريا.
3. To obtain potentiation (synergistic effect).   
 كثير التفاعل سائر مزدوج.   
 Ex: -B-lactams and aminoglycosides in endocarditis. Penicillin + Aminoglycosides
- 2 separate IV bolus injection, with time interval to avoid interaction.   
 - Co-trimoxazole.

\* لما الحريف في موضوع antibiotic سرعته diarrhea لازم يوقف antibiotic في موضوعه لأننا بتكون بتقل NF وبتزيد growth لا second bacteria متبعه superinfection.

### 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.   
 ممكن يضربوا على ضعف مثل ال tetracycline مع ال penicillin.
2. Suppression of normal flora, so give higher chance for opportunistic infection (superinfection).   
 البكتيريا بتسبب.
3. Increased incidence of adverse reactions.   
 ال superinfection علاجها.
4. Highly cost   
 أصعب من علاج البكتيريا العارضة بسبب ال original infection.



## 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)

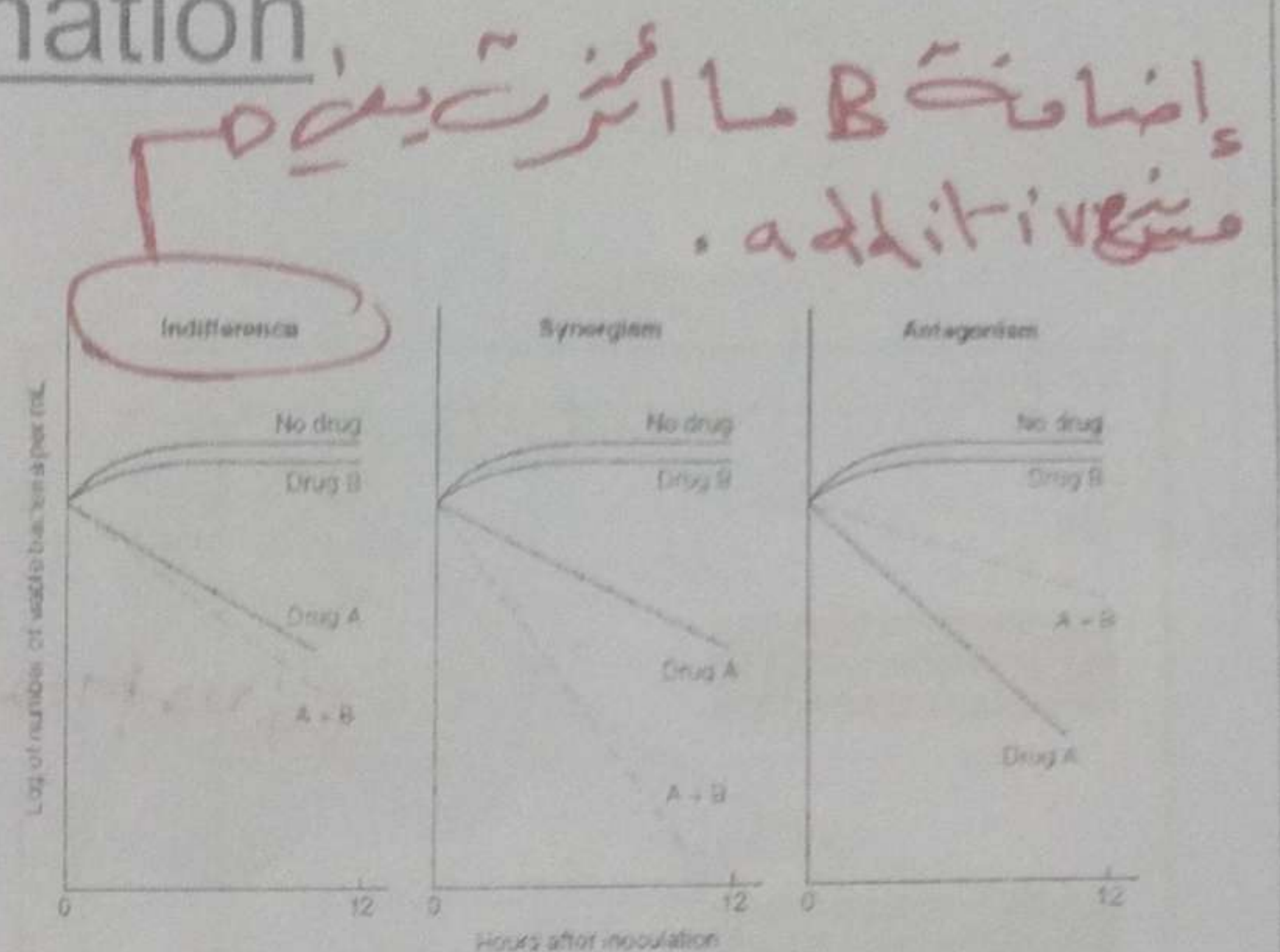
• بعضنا أداء بعض (بعضوا بعض)

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

• والص نفس التأثير صغير مضاعف

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

• بعضنا على بعض



• لما المريف يوقف كورس علاج لـ ١٥ أيام ويصير عليه ٥ أيام مثلاً  
يكون لصون صا Killing للبكتيريا ولكن فقط للبكتيريا الحساسة أما الـ  
resistant bacteria تكون لا موجودة ~~في~~ فلائنه وقف بهر لها  
growth وبعدين بهر لها Spreading

## Problems with antimicrobial agents

1. Drug resistance. (the major problem)   
علاش صليق عدم الحال الكورس  
resistance  
(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).

infection بالآتي ويتكون من other NF غير Killing NF موجودة بحالة طبيعية.

### How Effective is an Antibiotic

محدد من صفات antibiotic نفسه وليس البكتريا.

#### Concentration Dependent Killing

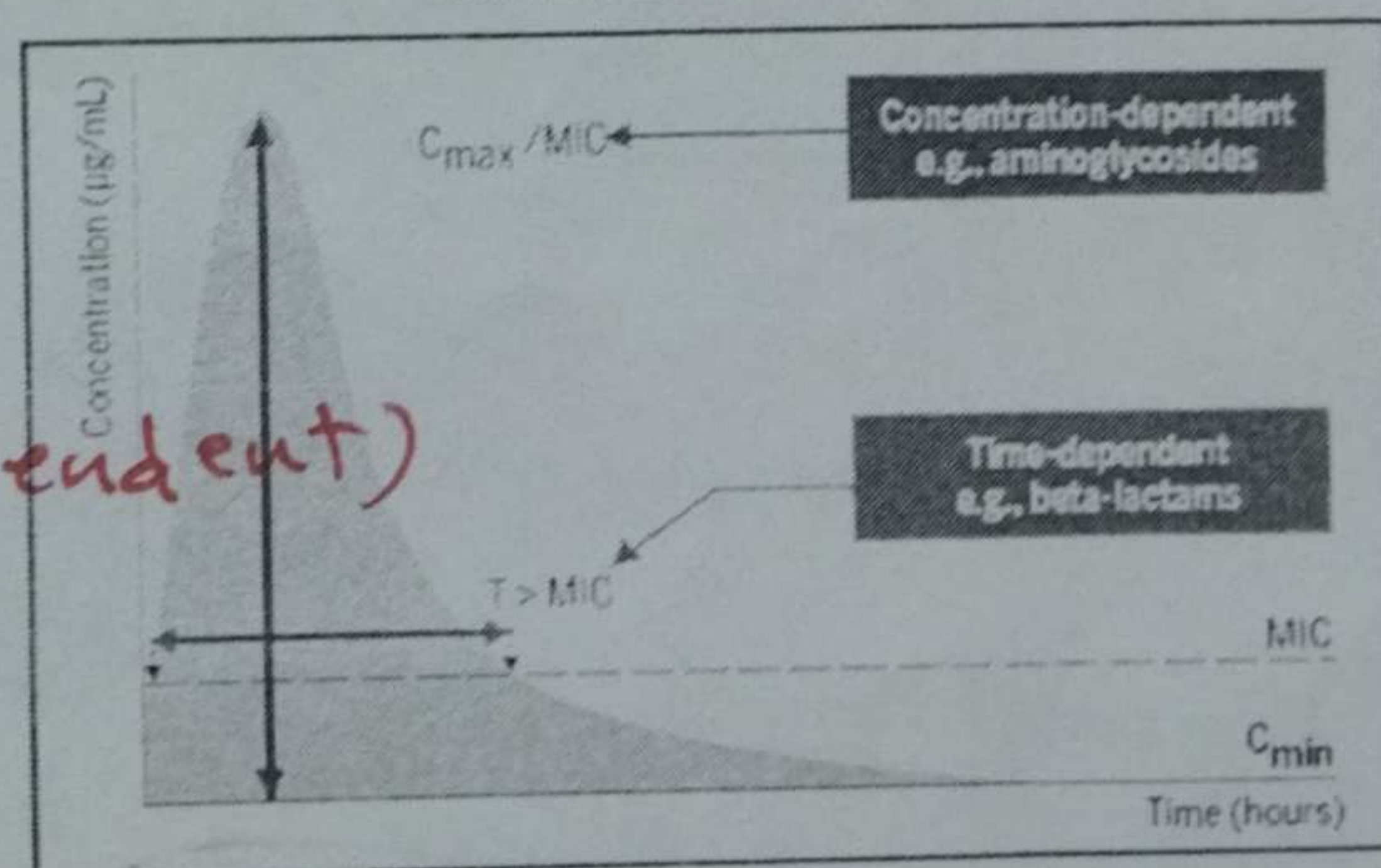
Efficacy determined by magnitude of serum concentration above MIC  
e.g. Aminoglycosides, quinolones.

#### Time Dependent Killing (conc: independent)

Efficacy determined by duration of time that serum concentrations exceed MIC

e.g. b-lactams, macrolides, cotrimoxazole

ANTIMICROBIAL AGENTS  
GENERAL PRINCIPLES



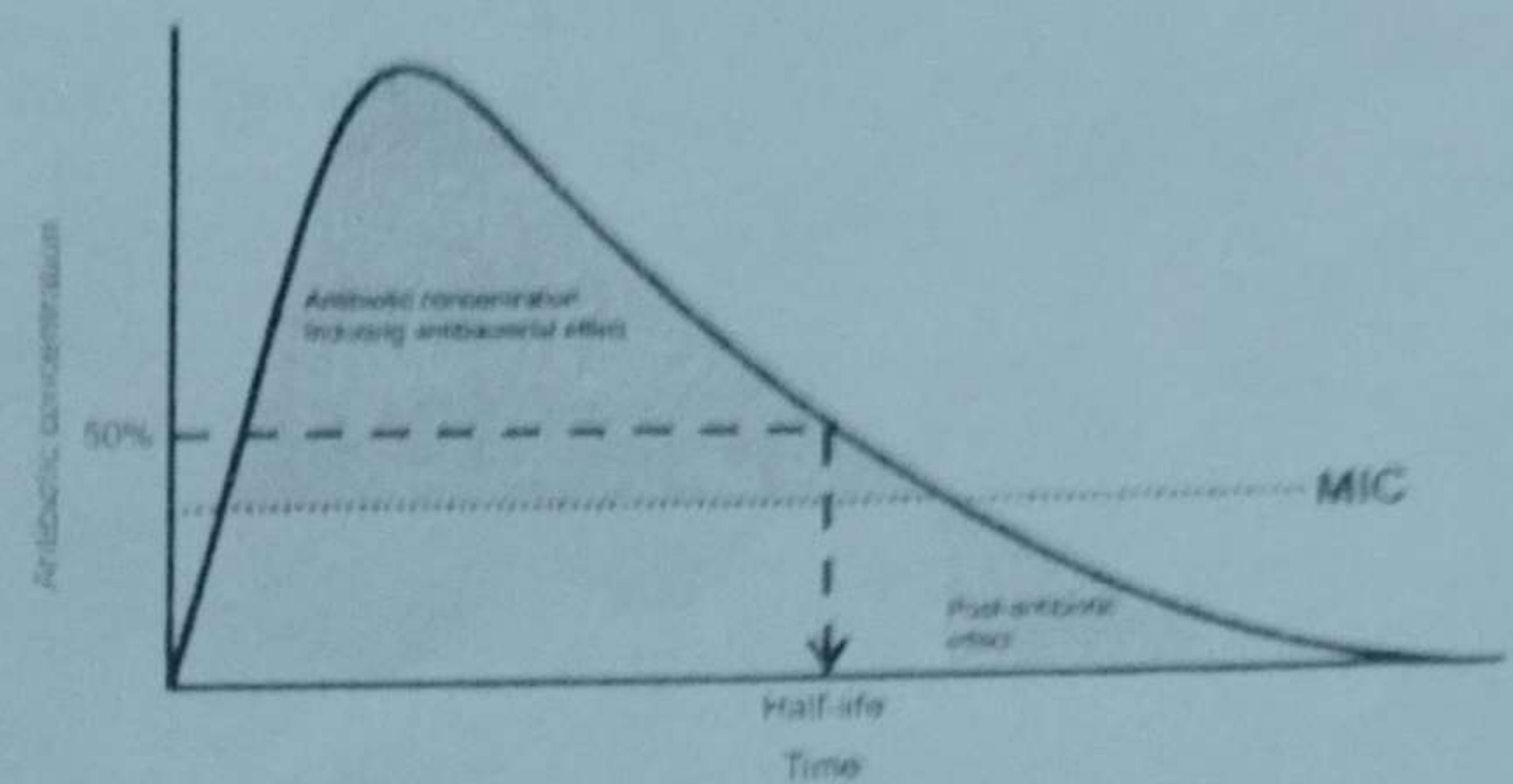


## How Effective is an Antibiotic

- **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