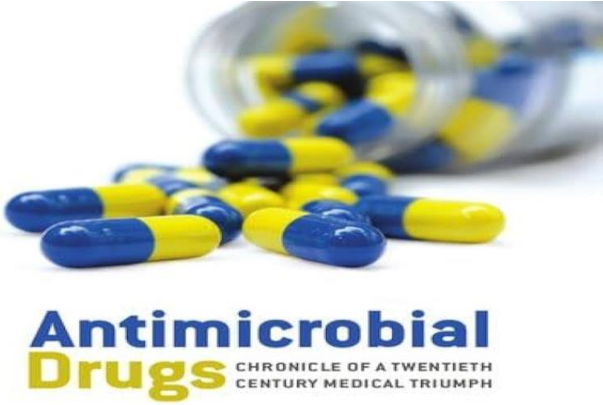


كلية التمريض – جامعة تكريت

المرحلة الثانية \ أدوية

أ د حسام الدين النجار

2024-2025 \ First Term

ANTIMICROBIAL CHEMOTHERAPY

- **Chemotherapy**
- Is the use of drugs with selective toxicity against pathogens such as bacteria, viruses, fungi, protozoa as well as cancer cells.
- It includes antibiotics, antifungal, antiviral, antiprotozoal, antihelminthic and anticancer.
- **Antibiotics:**

  Are substances produce by microorganisms that kill or inhibit the growth of other microorganisms. They include natural (penicillin G), semisynthetic or synthetic antibacterial agents (sulfonamides and quinolones).

ZIKA VIRUS

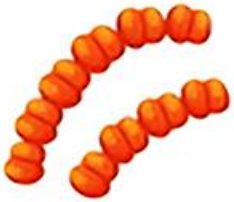
HPV

VIBRIO CHOLERAE

INFLUENZA

HANTAVIRUS

HEPATOVIRUS A



STREPTOCOCCUS THERMOPHILUS

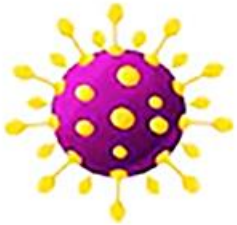
LACTOBACILLUS

PYROCOCCUS FURIOSUS

SALMONELLA

ADENOVIRUS

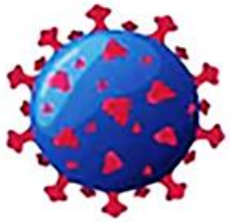
BACTERIOPHAGE



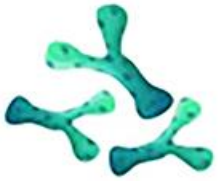
HERPES VIRUS

STAPHYLOCOCCUS AUREUS

EBOLA VIRUS



CORONAVIRUS



BIFIDOBACTERIUM

HELICOBACTER PYLORI

ESCHERICHIA COLI

PNEUMOCOCCUS

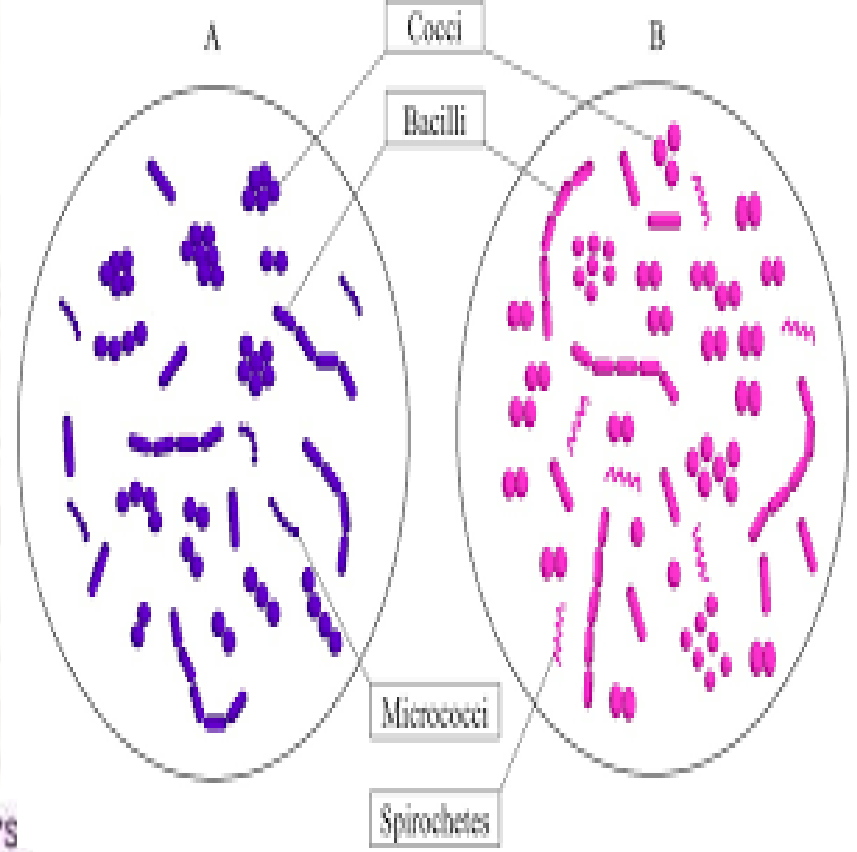
LACTOCOCCUS LACTIS

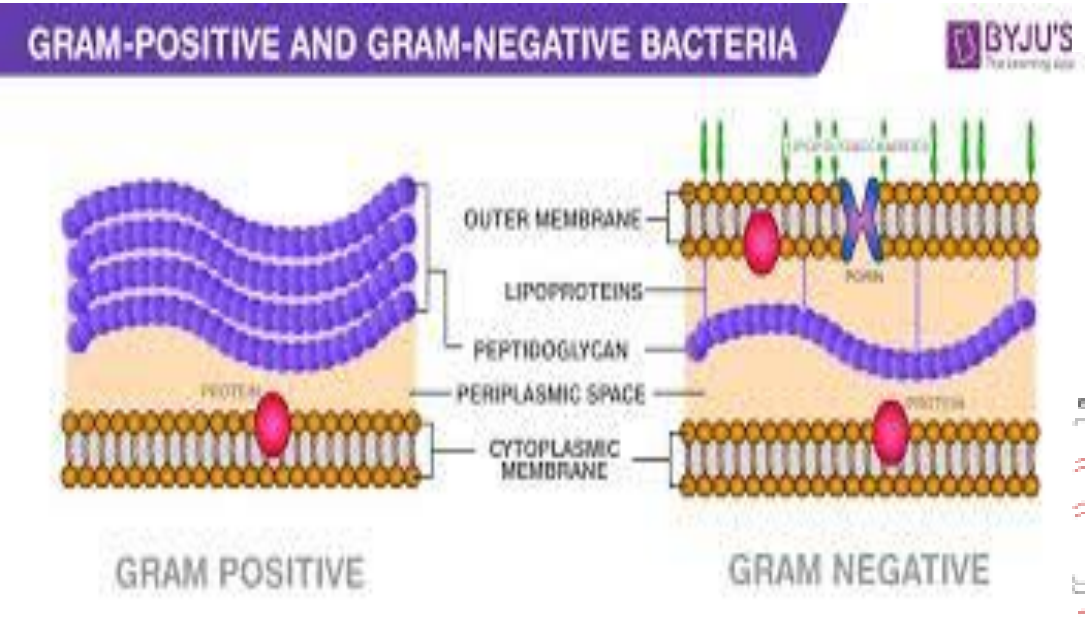
TETANUS VIRUS

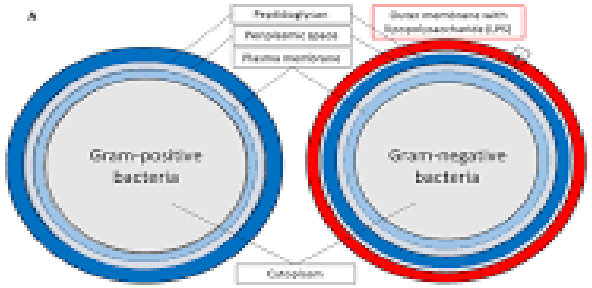
ANAPLASMA

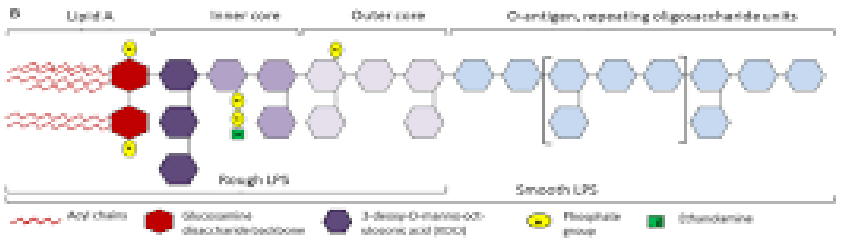
YERSINIA PESTIS


Here's everthing you must know about
GRAM POSITIVE
VS
GRAM NEGATIVE


A
Cocci
B
Bacilli
Micrococci
Spirochetes


GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA
BYJU'S
OUTER MEMBRANE
LIPOPROTEINS
PEPTIDOGLYCAN
PERIPLASMIC SPACE
CYTOPLASMIC MEMBRANE
PORIN
GRAM POSITIVE
GRAM NEGATIVE

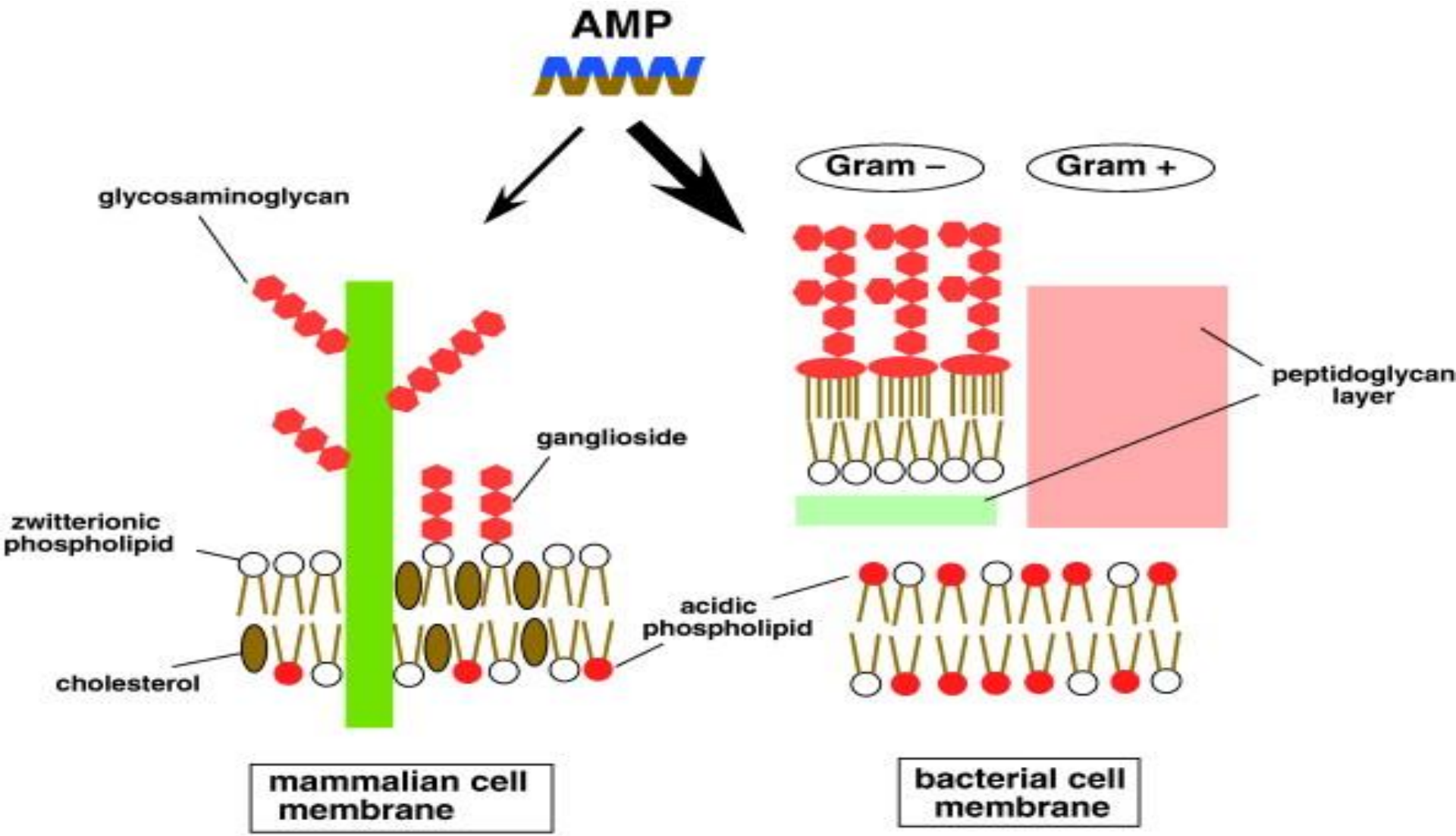

A
Peptidoglycan
Periplasmic space
Plasma membrane
Gram-positive bacteria
Gram-negative bacteria
Cytoplasm


B
Lipid A
Inner core
Outer core
O-antigen, repeating oligosaccharide units
Rough LPS
Smooth LPS
Acyl chains
Glucosamine
Phosphate group
Ethanolamine

- **Selective toxicity:**

- The drug interfere with the vital function of the organism without affecting the host (biochemical differences).
- e.g Bacterial cell wall (contains peptidoglycan) is a target for cell wall synthesis inhibitors.
- Bacterial ribosome (consists of 50S & 30S subunits whereas mammalian ribosome consists of 60S & 40S subunits) is a target of bacterial protein synthesis inhibitors.
- The folate synthesis is a metabolic pathway found in bacteria but not in human (target for antifolates).
- Cell membrane in bacteria can be more easily disrupted than in mammalian cell (polymixins).

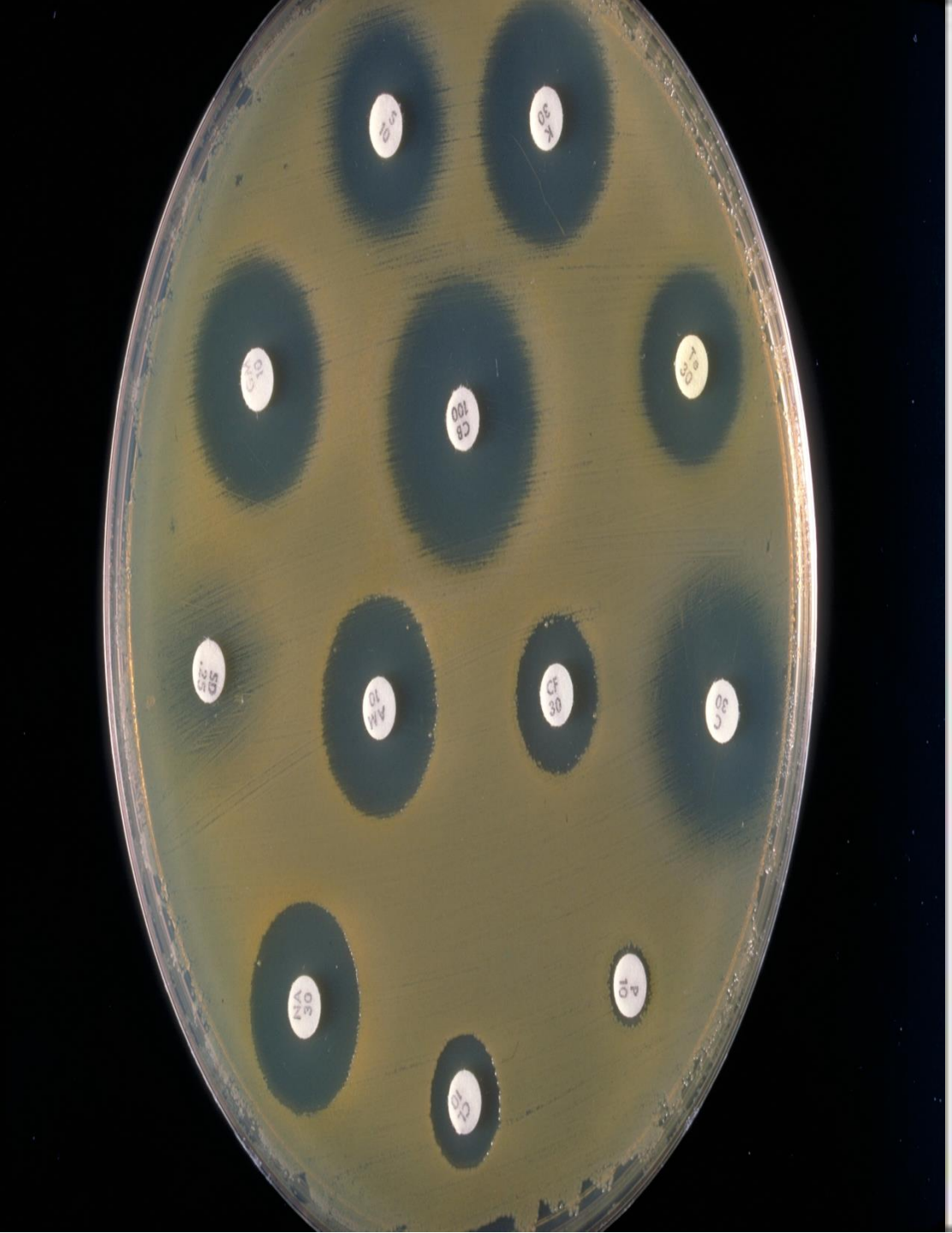
Selective toxicity between mammalian cell & bacterial cell

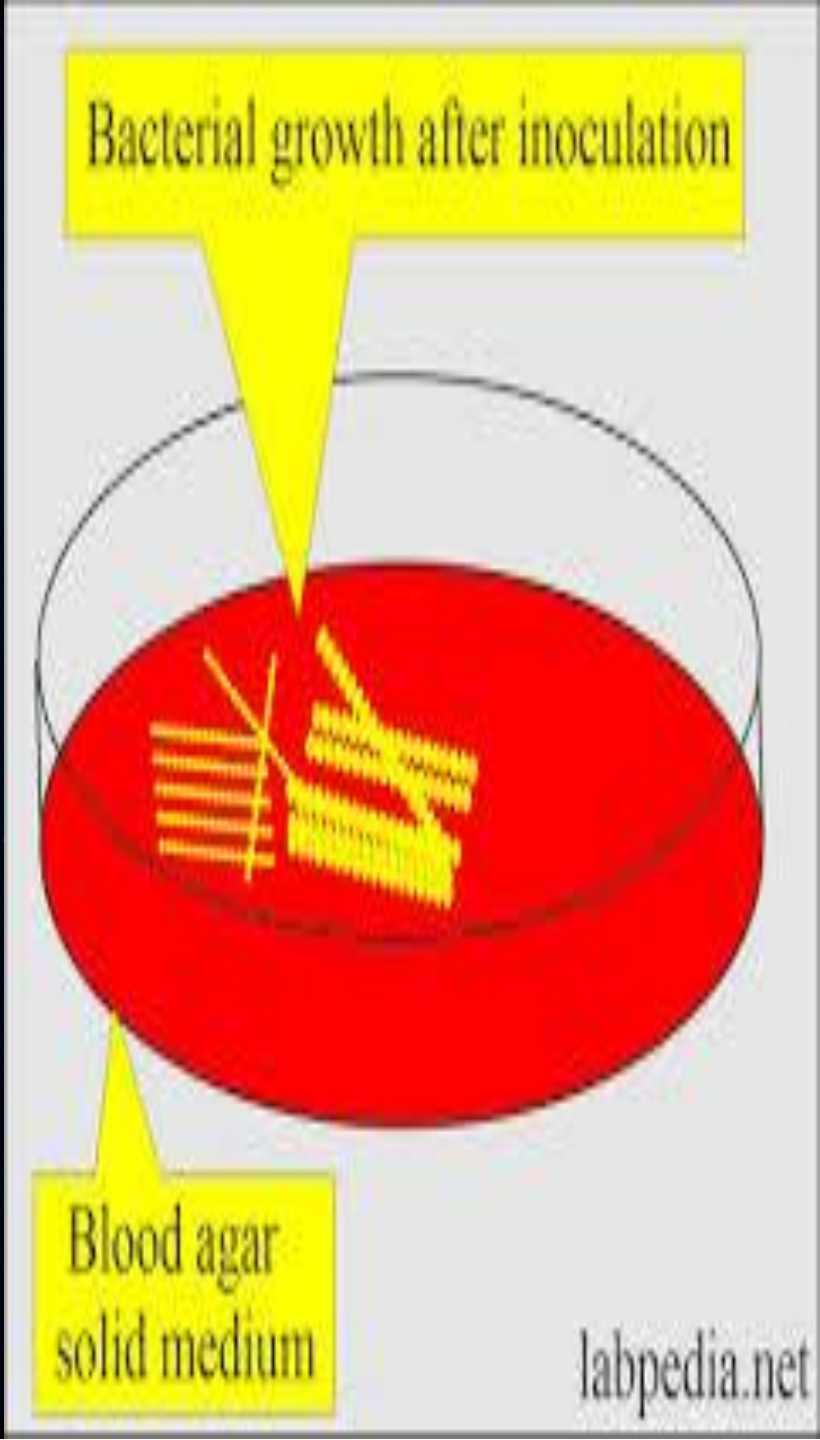


- **Selection of the appropriate antimicrobial agent**

Selection based on:

1. The organism's identity.
2. The sensitivity of the microorganism to a particular agent.
3. The site of the infection and the ability of the drug to reach that site.
4. Patient factors.
5. The safety of the antimicrobial agent.
6. The cost of therapy


P 10
K 30
OFX 5
CTX 30
CE 100
LEV 5
SXT 25
AM 10
CF 30
C 30
NA 30
P 10
CD


Bacterial growth after inoculation
Blood agar
solid medium
labpedia.net

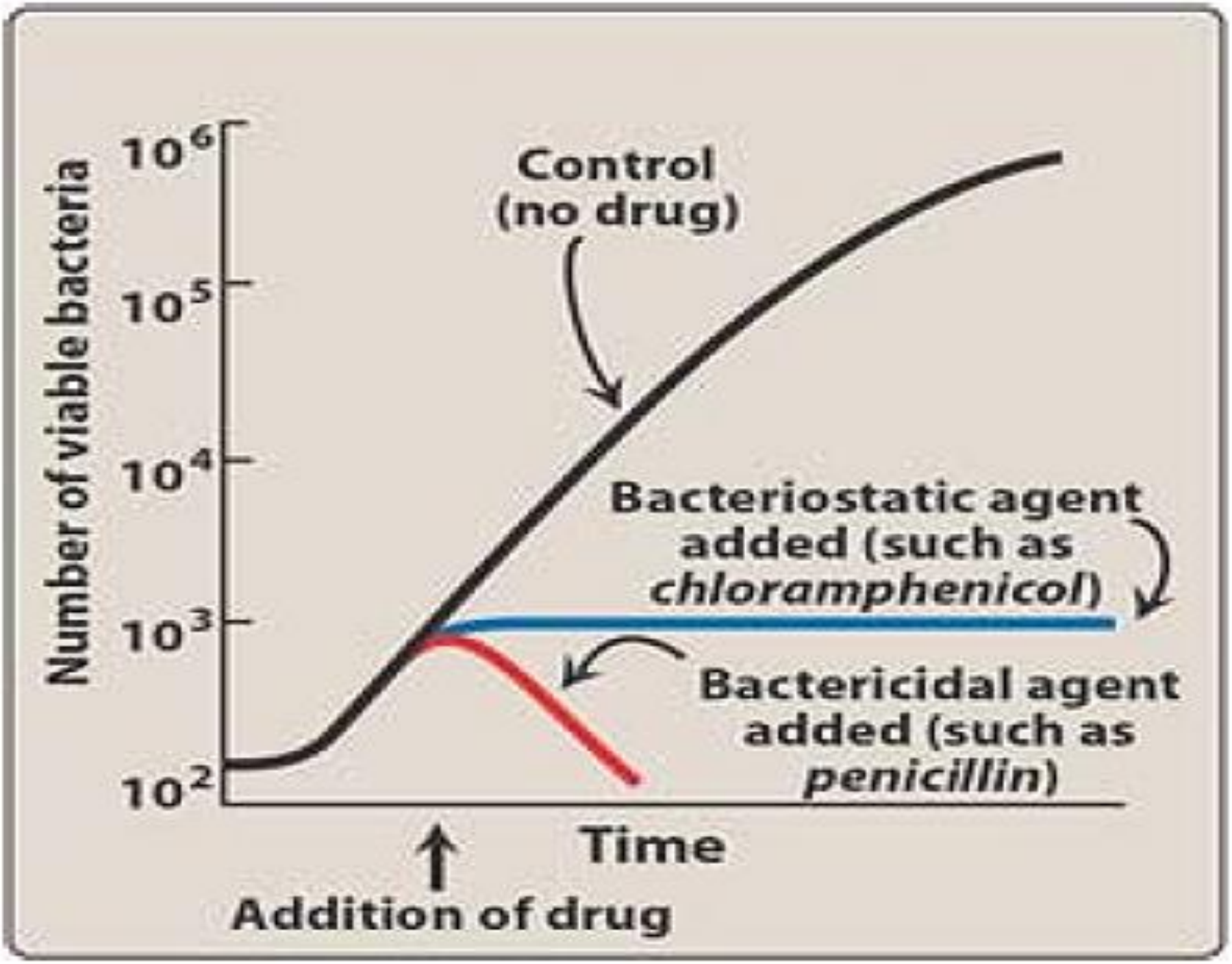
1. **Identification of the infecting organism:**

- Direct microscopic visualization (Gram Stain).
- Cultivation, identification and determination of the susceptibility of the infecting agent to drugs
- **Additional laboratory techniques:**
- Detection of microbial antigen
- Detection of microbial DNA or RNA
- Detection of an inflammatory or host immune response to the microorganism.

- **Empiric therapy prior to organism identification:**
  - Ideally, the antimicrobial agent is selected after identification of the microorganism and its drug sensitivity has been established.
  - Empiric therapy is started with a combination of antibiotics or a single drug covering infections by both G-ve, G+ve and anaerobic microorganisms.
  - Empiric therapy is indicated in following conditions:
  - Critically ill patient: with infections of unknown origin.
  - Neutropenic patient.
  - Patient with symptoms indicative for meningitis.

2. **The sensitivity of the microorganism to a particular agent.**

- **Minimum inhibitory concentration (MIC):** Is the lowest concentration of antibiotic that inhibits bacterial growth.
- **Minimum bactericidal concentration (MBC):** Is the lowest concentration of antibiotic that kills 99.9 percent of bacterial .
- **Bacteriostatic antibiotics:** Drugs that arrest the growth and replication of bacteria at serum levels achieved clinically, thus limiting the spread of infection while the immune system acts to eliminates the pathogen.
- **Bactericidal antibiotics:** are drugs that kill bacteria at drug serum levels achieved clinically (drugs of choice in seriously ill patients).


Number of viable bacteria
10^6
10^5
10^4
10^3
10^2
Control
(no drug)
Bacteriostatic agent
added (such as
chloramphenicol)
Bactericidal agent
added (such as
penicillin)
Time
Addition of drug

3. **The site of the infection:**

- Adequate concentration of the antibiotic must be reached at the site of infection for effective eradication of the infecting organism
- **The Blood Brain Barrier:**
- If infection is in the CSF, polar drugs and drugs highly bound to plasma proteins have ↓activity (↓penetration).

4. Patient factors:

- The patients immune system status, kidneys and liver function, circulation, age, pregnancy and breast feeding should be considered when selecting an antimicrobial drug.

A. Immune system:

- Alcoholism, diabetes, HIV infection, malnutrition and advanced age as well as therapy with immunosuppressant drugs can affect a patient's immunity.
- Higher-than-usual doses of bactericidal agents or longer courses of treatment are require in these individuals.

B. **Renal function:**

- Dosage adjustment is needed in patient with renal dysfunction to prevent serious adverse effects resulting from drug accumulation.

C. **Hepatic dysfunction:**

- Antibiotics that are concentrated or eliminated by the liver (Erythromycin and Tetracyclines) are contraindicated in patients with liver disease.

D. **Poor perfusion:**

- Decreased circulation to an anatomic area, such as the lower limbs of a diabetic, reduces the amount of antibiotic that reaches that area

E. **Age:**

- Renal or hepatic elimination processes are often poorly developed in newborns
- Chloramphenicol and sulfonamides → toxic effects in neonates. Tetracyclines affect bone growth in young children.

F. **Pregnancy:**

- All antibiotics cross the placenta.
- Adverse effects to the fetus include:
- Tooth dysplasia and inhibition of bone growth encountered with the tetracyclines.
- Some anthelmintics are embryotoxic and teratogenic.
- Aminoglycosides are ototoxic to the fetus.
- All drugs during pregnancy should be used only under the supervision of a patient's physician.

FDA Pregnancy Drug Risk Information

Category A

Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).

Example drugs or substances: levothyroxine, folic acid, liothyronine.

Category B

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Example drugs: metformin, hydrochlorothiazide, amoxicillin.

Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Example drugs: gabapentin, amlodipine, trazodone.

Category D

There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

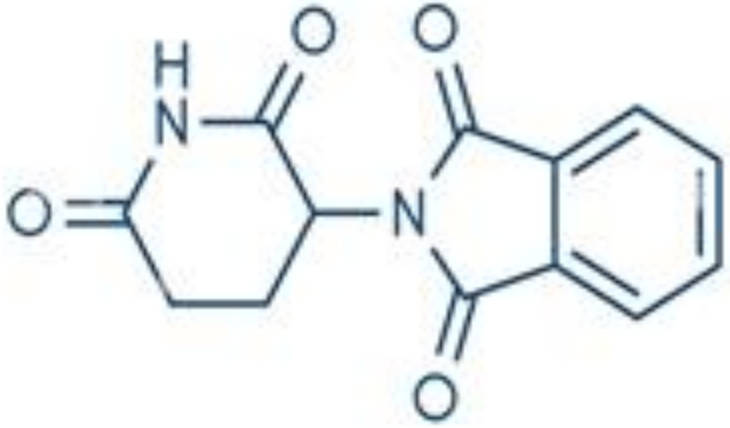
Example drugs: losartan

Category X

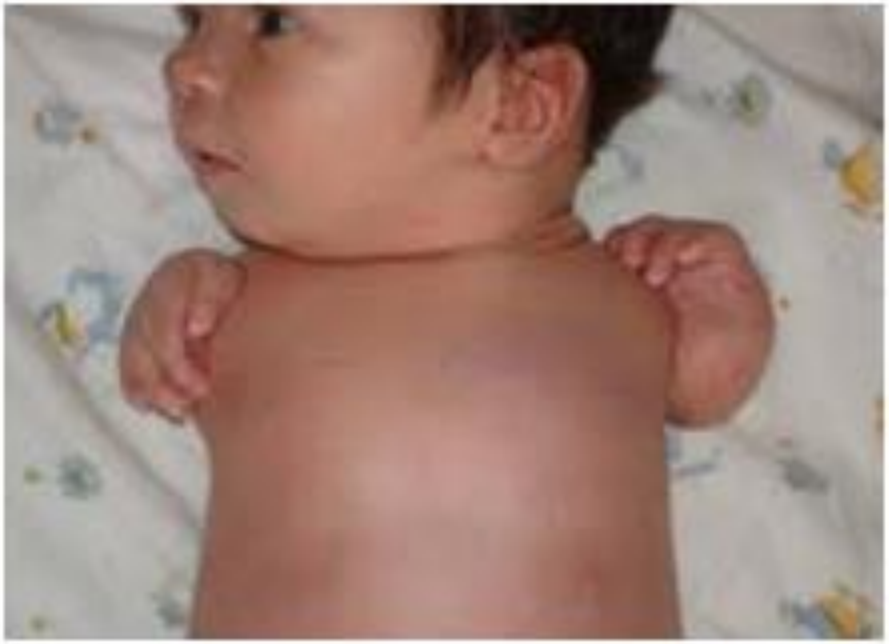
Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Example drugs: atorvastatin, simvastatin, methotrexate, finasteride.

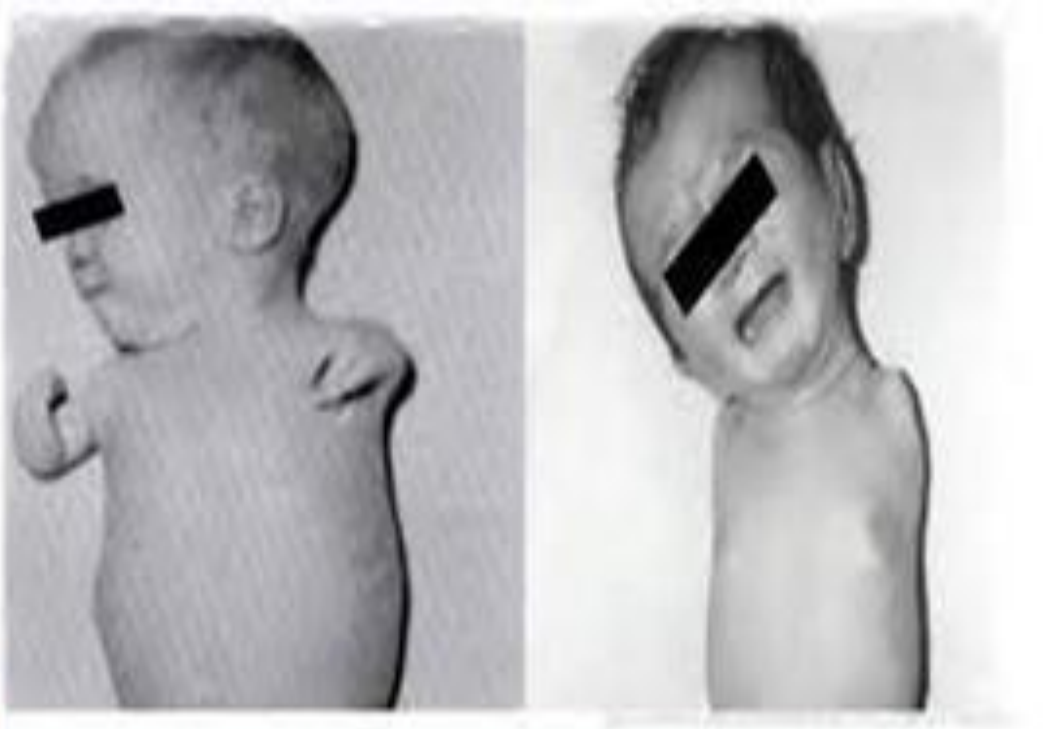
CATE-GORY	DESCRIPTION	DRUG
A	No human fetal risk or remote possibility of fetal harm	
B	No controlled studies show human risk; animal studies suggest potential toxicity	β-Lactams β-Lactams with inhibitors Cephalosporins *Aztreonam* *Clindamycin* *Erythromycin* *Azithromycin* *Metronidazole* *Nitrofurantoin* Sulfonamides
C	Animal fetal toxicity demonstrated; human risk undefined	*Chloramphenicol* Fluoroquinolones *Clarithromycin* *Trimethoprim* *Vancomycin* *Gentamicin* *Trimethoprim-sulfa-methoxazole*
D	Human fetal risk present, but benefits outweigh risks	Tetracyclines Aminoglycosides (except *gentamicin*)
X	Human fetal risk present but does not outweigh benefits; contraindicated in pregnancy	

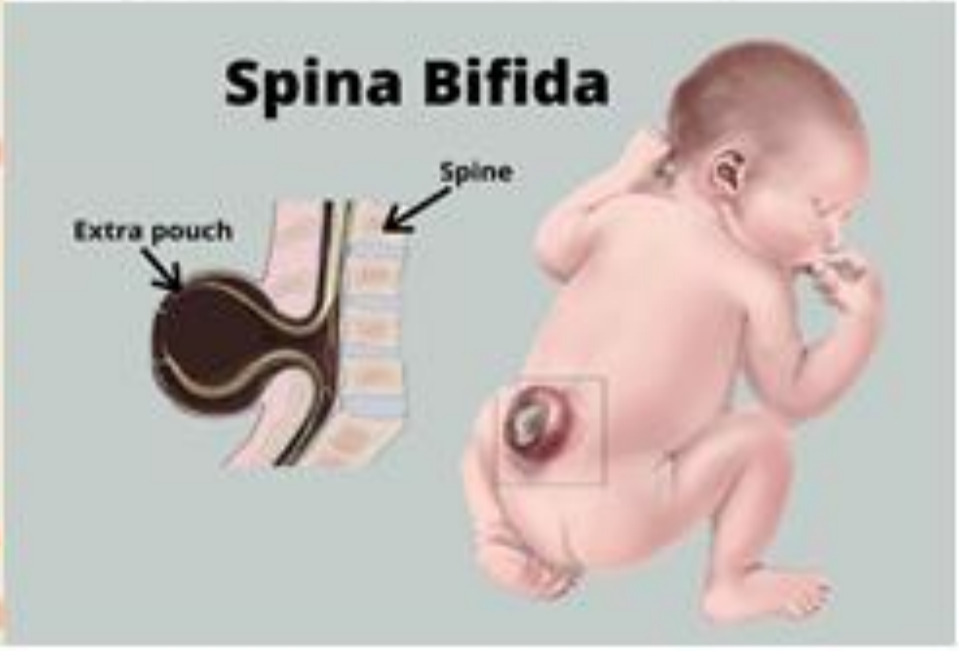


thalidomide




(A)
(B)




Spina Bifida
Spine
Extra pouch

G. **Lactation**:

- Drugs administered to a lactating mother may enter the nursing infant via the breast milk.
- Although the concentration of an antibiotic in breast milk is usually low, the total dose to the infant may be enough to cause problems.

5. The safety of the antimicrobial agent:

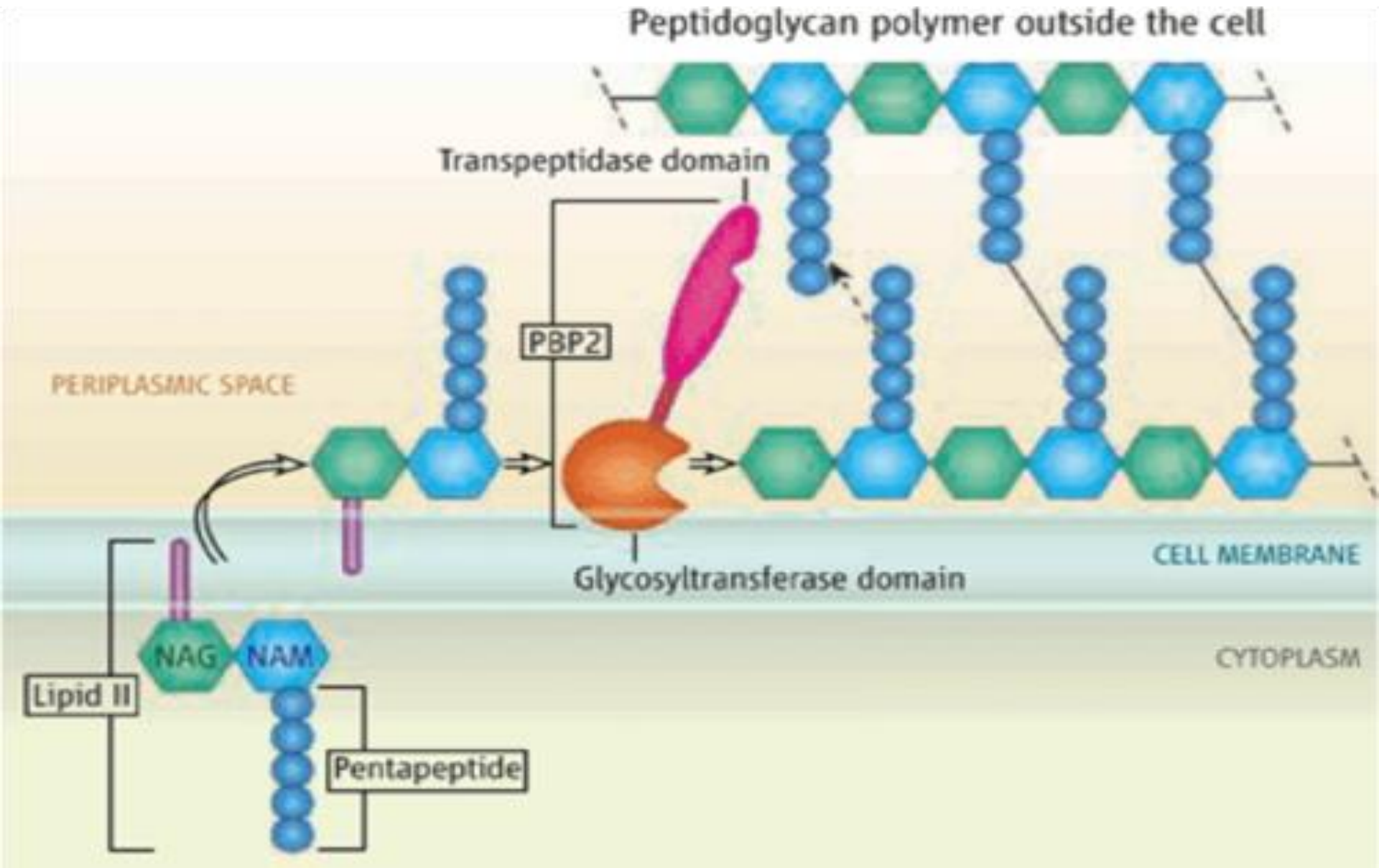
- Many of the antibiotics (penicillins) are among the least toxic of all drugs (↑ selective to microorganisms)
- Other antimicrobial agents (chloramphenicol) are less microorganism specific and are associated with serious toxicity to the patient.
- Drugs with serious adverse effects are generally reserved for life-threatening infections.
- Safety is related not only to the nature of the drug but also to patient factors that can predispose to toxicity.

Classification of Antibiotics

- Classified according to mechanism of action.

1. **Inhibitors of cell wall synthesis:**
   β-Lactams , Vancomycin, Cycloserine, Bacitracin and Fosfomycin
2. **Inhibitors of cell membrane function**.
   Isoniazid and Amphotericin B.
3. **Inhibitors of protein synthesis**.
   Tetracyclines, Macrolides, Chloramphenicol, Aminoglycosides and Clindamycin.
4. **Inhibitors of bacterial metabolism.**
   Sulfonamides and Trimethoprim
5. **Inhibitors of nucleic acid synthesis or function**.
   Fluoroquinolones and Rifampin.

PENICILLIN BINDING PROTEIN

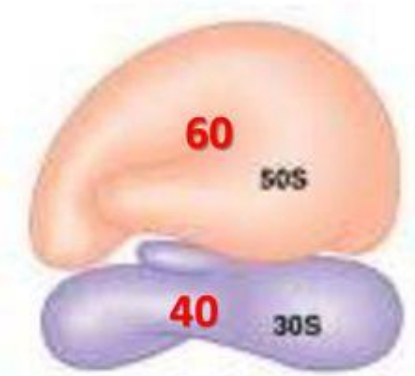


Protein Synthesis Inhibitors

- Targeting **the bacterial ribosome**, which has components that differ structurally from those of the mammalian cytoplasmic ribosome.

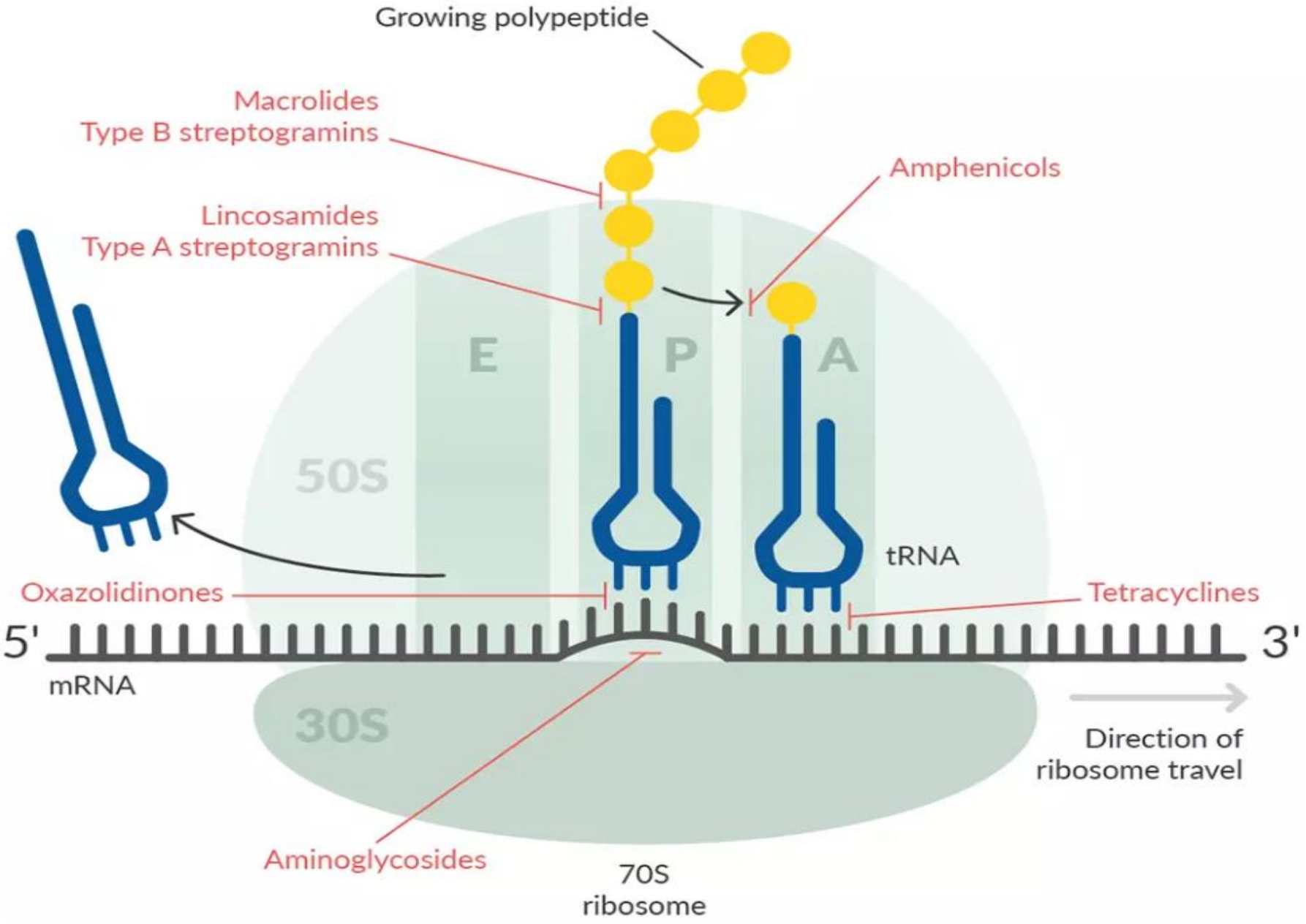
- The bacterial ribosome:
  - is smaller (70S) than the mammalian ribosome (80S)
  - composed of 50S and 30S subunits

- Mammalian ribosomes
  - 80S
  - Composed of 60S and 40S subunits.



(c) Complete 70S ribosome

80S ribosome (human)


Growing polypeptide
Macrolides
Type B streptogramins
Lincosamides
Type A streptogramins
Amphenicols
E
P
A
50S
tRNA
Oxazolidinones
Tetracyclines
5'
3'
mRNA
30S
Direction of
ribosome travel
Aminoglycosides
70S
ribosome

- **Classification of antimicrobial agents**:

According to their chemical structure:

- β-lactams, sulphonamides, aminoglycosides, macrolides.

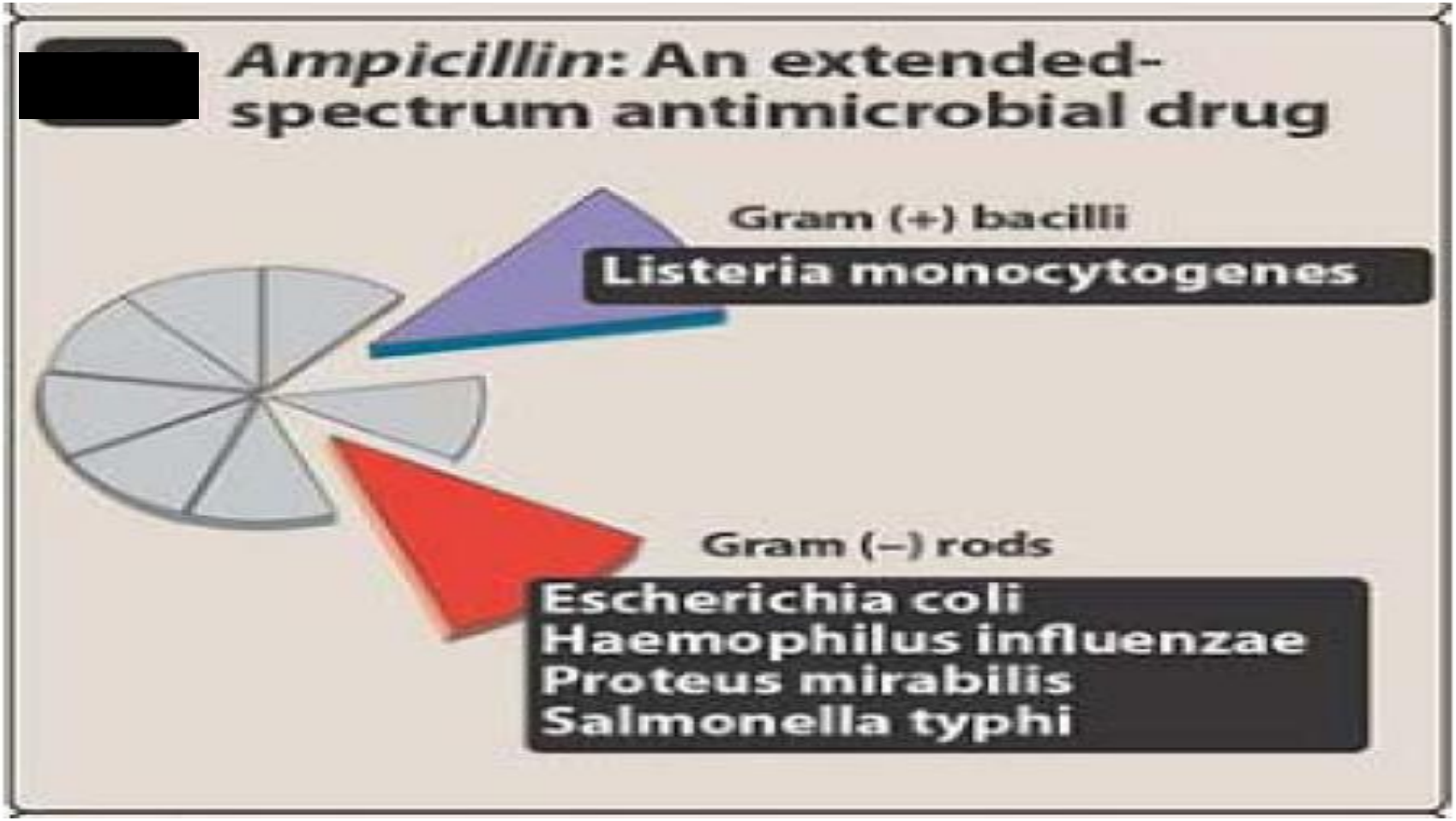
According to their chemotherapeutic spectra:

A. **Narrow-spectrum antibiotics:**

- Chemotherapeutic agents acting
- only on a single or a limited group
- of microorganisms (Isoniazid is
- active only against mycobacteria)

B. Extended-spectrum antibiotics:

Are antibiotics that are effective against G+ve and also against a significant number of G-ve bacteria.



C. Broad-spectrum antibiotics:

- Drugs such as tetracycline and chloramphenicol affect a wide variety of microbial species. For example tetracycline is effective against: G-ve rods, anaerobic organism, spirochetes, mycoplasma, chlamydia, actinomyces and rickettsiae and amoebae.
- Administration of broad-spectrum antibiotics can drastically alter the nature of the normal bacterial flora and precipitate a superinfection of an organism such as Candida albicans.

- **Combinations of Antimicrobial Drugs:**
- **Advantages:**

1. To avoid the development of resistance (Tuberculosis)
2. To treat mixed bacterial infection .
3. Synergism and potentiating of antibacterial activity:

- Sulfamethoxazole & trimethoprim
- Penicillins & gentamicin

4. When the greatest antimicrobial coverage is required (sepsis, meningitis and in empirical therapy in which the causative agent has not been identified

- **Disadvantages**

1. Risk of toxicity
2. Antagonistic effect:

- Bacteriostatic drugs antagonize the action of bactericidal agents (bactericidal antibiotics act only when organisms are multiplying)
- For example, bacteriostatic tetracycline drugs may interfere with the bactericidal effect of penicillins and cephalosporins

ANY QUESTIONS ?