



PRINCIPLES OF ANTIMICROBIAL THERAPY

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OBJECTIVES

- TO EXPLAIN GENERAL PRINCIPLES OF ANTIBIOTICS
- TO CLASSIFY ANTIBIOTICS
- TO DESCRIBE AND UNDERSTAND MECHANISMS OF ACTION OF ANTIBIOTICS.
- GENERAL SIDE EFFECTS OF ANTIBIOTICS
- CLINICAL APPROACH TO PRESCRIBE ANTIBIOTICS

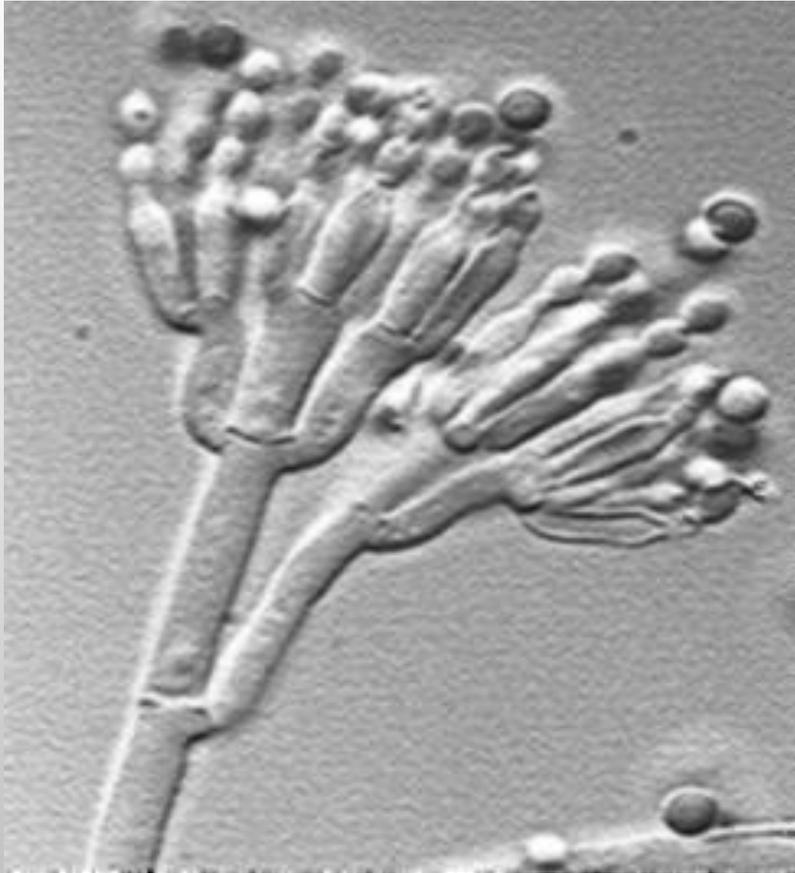
WHAT ARE ANTIBIOTICS?

- IS A SUBSTANCE PRODUCED BY LIVING MICRO-ORGANISMS TO INHIBIT OR KILL ANOTHER LIVING MICRO-ORGANISMS E.G: PENICILLINS, CEPHALOPORINS , TETRACYCLINES AND CHLORAMPHICOL.
- **ANTIMICROBIAL AGENT:**
- IS ANY CHEMICAL SUBSTANCE WHICH KILLS THE ORGANISM OR INHIBITS ITS GROWTH E.G: SULPHONAMIDES, QUINOLONES
- TODAY THE TERM ANTIBIOTICS EXTENDS TO INCLUDE **SYNTHETIC ANTIBACTERIAL AGENTS:** SULFONAMIDES AND QUINOLONES

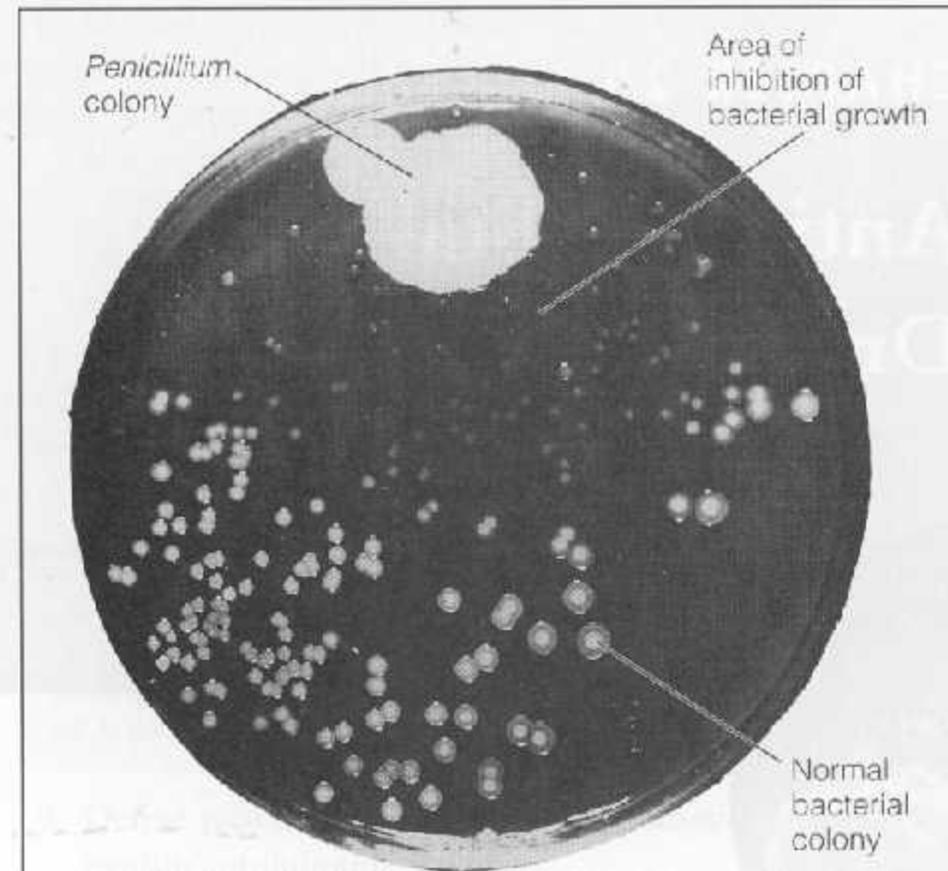
CLASSIFICATION OF ANTIBIOTICS ACCORDING TO SOURCE

- 1- NATURAL: SEVERAL SPECIES OF FUNGI INCLUDING *PENICILLIUM* AND *CEPHALOSPORIUM*
- E.G. PENICILLIN, CEPHALOSPORIN
- NEW SOURCES EXPLORED: PLANTS, HERPS, FISH
- 2- SYNTHETIC: SULPHA DRUGS
- 3- SEMISYNTHETIC: AMPICILLIN

SIR ALEXANDER FLEMING



FLEMING'S PETRI DISH



SELECTIVE TOXICITY

- TO BE EFFECTIVE AND SAFE, ANTIMICROBIAL AGENT MUST HAVE **SELECTIVE TOXICITY**
- SELECTIVE TOXICITY IS DUE TO THE DIFFERENCE IN STRUCTURE AND/OR METABOLISM BETWEEN THE PATHOGEN AND THE HOST.

PROKARYOTIC CELL	EUKARYOTIC CELL
Generally smaller in size than the eukaryotic cell (1-10 μ m)	Larger in size than the prokaryotic cell (5-100 μ m)
Membrane bound organelles are absent.	Membrane bound organelles are present.
The chromosome is singular.	More than one chromosomes are present.
The nuclear region is not very well defined and is called as the nucleoid.	The nuclear region is very well defined in form of separate membrane bound organelle called as the nucleus.

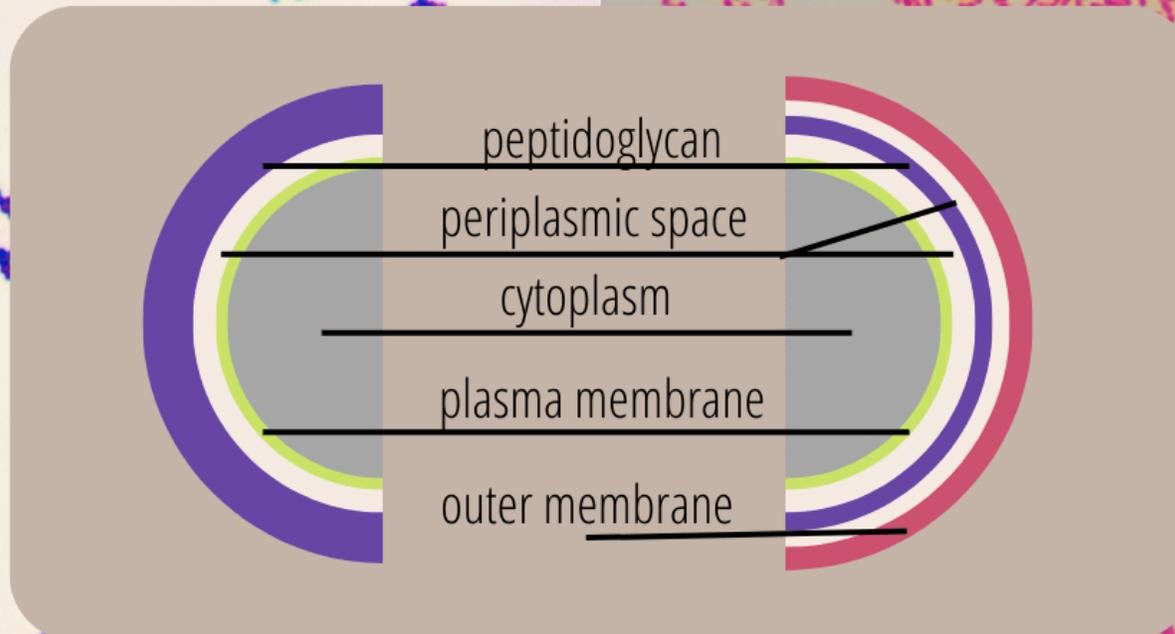
GRAM POSITIVE & GRAM NEGATIVE

- GRAM POSITIVE BACTERIA HAVE A THICK CELL WALL
 - PEPTIDOGLYCAN DIRECTLY ACCESSIBLE FROM ENVIRONMENT
- GRAM NEGATIVE BACTERIA HAVE A DIFFERENT WALL
 - THIN LAYER OF PEPTIDOGLYCAN
 - SURROUNDED BY AN **OUTER MEMBRANE** COMPOSED OF LIPOPOLYSACCHARIDE, PHOSPHOLIPIDS, AND PROTEINS
 - OUTER MEMBRANE IS A BARRIER TO DIFFUSION OF MOLECULES INCLUDING MANY ANTIBIOTICS
 - SOME LIPOPHILIC ANTIBIOTICS MAY DIFFUSE IN.
 - PORINS ALLOW PASSAGE OF ONLY SOME ANTIBIOTICS

Gram Positive vs Gram Negative Bacteria

Gram Positive

Gram Negative



ANTIBIOTICS ACCORDING TO THEIR MODE OF ACTION

- BACTERIOSTATIC VS. BACTERICIDAL
- ANTIBIOTICS DIFFER BY MODE OF ACTION
- BACTERIOSTATIC COMPOUNDS **INHIBIT THE GROWTH OF BACTERIA**
- HOST IMMUNE SYSTEM DOES THE KILLING
- BACTERICIDAL COMPOUNDS **DIRECTLY KILL THE BACTERIA**
- **BACTERIOSTATIC & CIDAL:**
- ACCORDING TO CONCENTRATION E.G: ERYTHROMYCIN AND ISONIAZIDE.
- LOCATION AND SEVERITY OF INFECTION AFFECT CHOICE OF ANTIBIOTIC
 - E.G. CNS INFECTION CALLS FOR BACTERICIDAL TREATMENT.

ANTIBIOTICS ACCORDING TO THE SPECTRUM

- **BROAD SPECTRUM:**
- EFFECTIVE AGAINST MULTIPLE GRAM +VE & -VE ORGANISMS E.G: EMEPENEM, TETRACYCLINE, QUINOLONES ,CHLORAMPHICOL.
- USED AS INITIAL EMPIRICAL TREATMENT TILL CULTURE AND SENSITIVITY RESULTS APPEAR.
- **NARROW SPECTRUM**
- EFFECTIVE AGAINST SPECIFIC ORGANISMS E.G: ANTIMICROBIAL AGAINST GRAM +VE BACTERIA: VANCOMYCIN AND PENICILLIN G.
- ANTIMICROBIAL AGAINST GRAM -VE BACTERIA: POLYMXINE, BACITRACIN AND AMINOGLYCOSIDES.
- USED IN TREATMENT OF SUSCEPTIBLE ORGANISMS BASED ON CULTURE AND SENSITIVITY RESULTS.
- **MODERATE SPECTRUM:** E.G: MACROLIDS

EXTENDED-SPECTRUM ANTIBIOTICS

- EXTENDED SPECTRUM IS THE TERM APPLIED TO ANTIBIOTICS THAT ARE MODIFIED TO BE EFFECTIVE AGAINST GRAM-POSITIVE ORGANISMS AND ALSO AGAINST A SIGNIFICANT NUMBER OF GRAM-NEGATIVE BACTERIA.
- FOR EXAMPLE, *AMPICILLIN*

- **GRAM-POSITIVE AND GRAM-NEGATIVE COVERAGE**
- **ALL BUT 4 OF THE ANTIBIOTIC CLASSES** COVER BOTH GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA.
- **SPECIFIC COVERAGE CLASSES**
- THE 4 CLASSES THAT HAVE SPECIFIC GRAM COVERAGE INCLUDE GLYCOPEPTIDES, LINCOSAMIDES, AMINOGLYCOSIDES, AND MACROLIDES (**GLAM**).

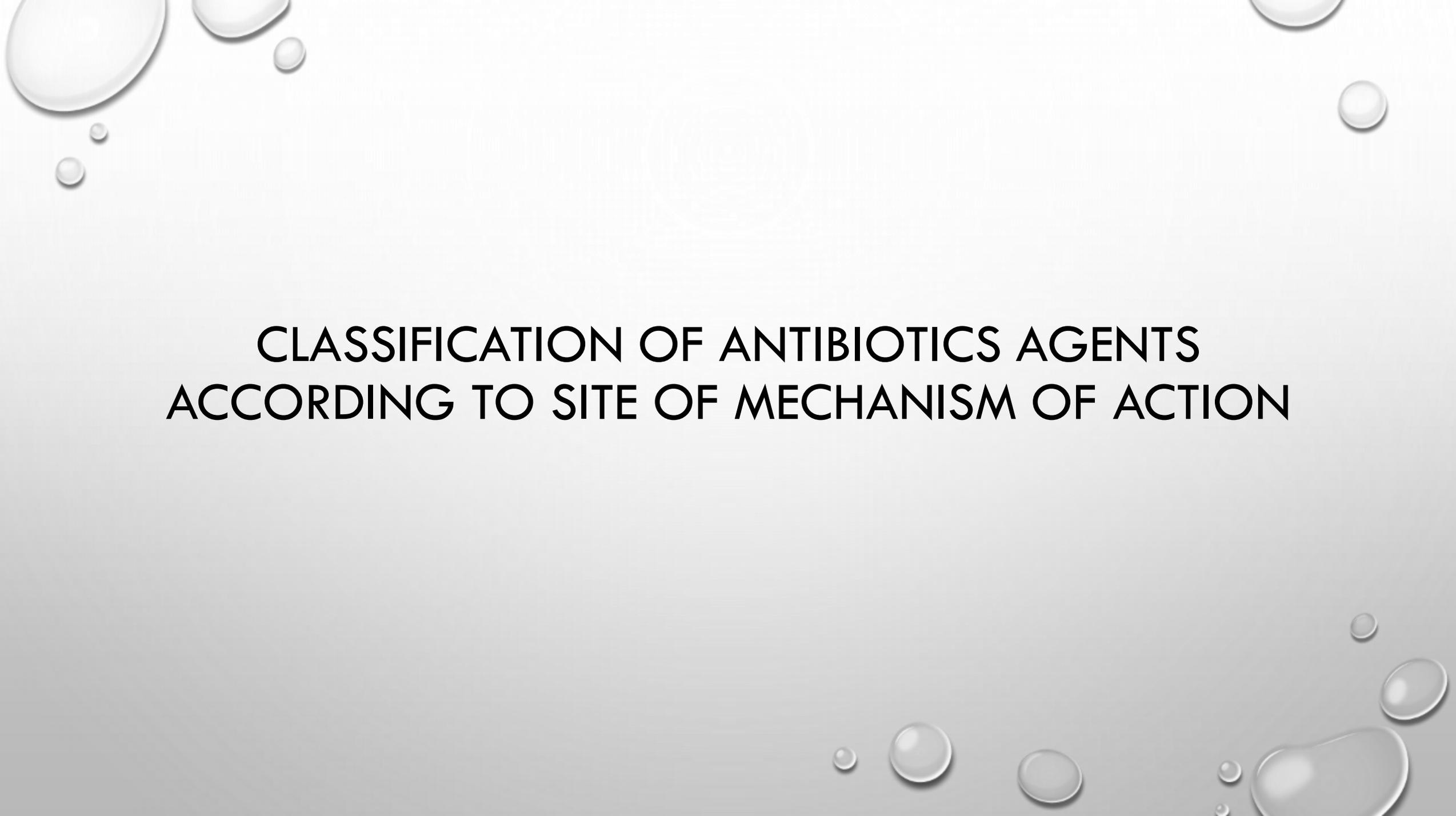
- **GRAM-NEGATIVE COVERAGE ONLY**

- AMINOGLYCOSIDES PRIMARILY COVER GRAM-NEGATIVE BACTERIA (WITH SOME MINOR EXCEPTIONS AGAINST GRAM-POSITIVES, ESPECIALLY WHEN USED SYNERGISTICALLY).

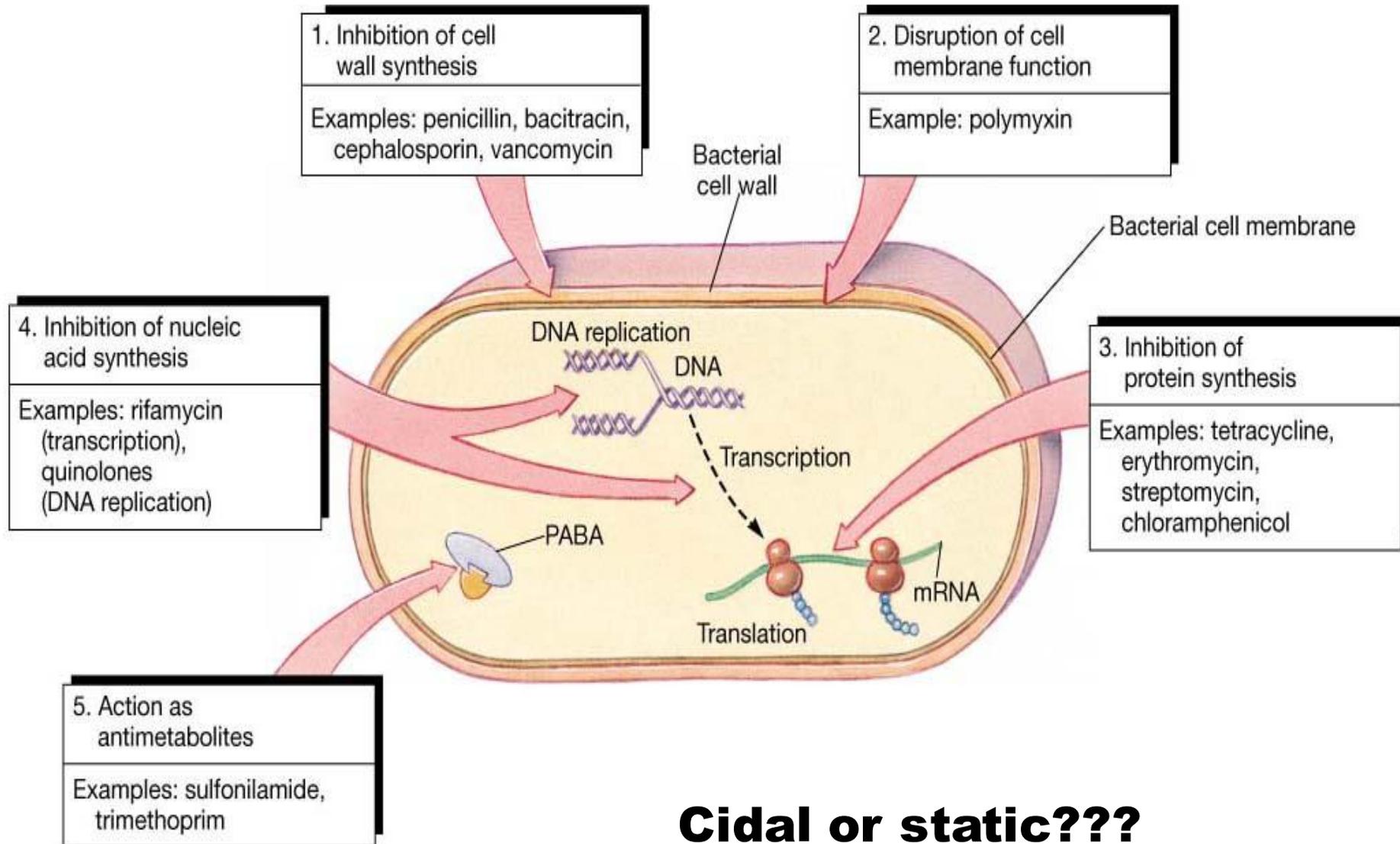
- THE WORD AMINOGLYCOSIDE HAS THE WORD “**NO**” IN IT. NO IS A NEGATIVE RESPONSE WHICH WILL HELP YOU REMEMBER GRAM-NEGATIVE.

- **GRAM-POSITIVE COVERAGE ONLY**

- THE OTHER 3 CLASSES (GLYCOPEPTIDES, LINCOSAMIDES, AND MACROLIDES) PRIMARILY COVER GRAM-POSITIVE BACTERIA ONLY (WITH MACROLIDES HAVING MINOR GRAM-NEGATIVE COVERAGE AS WELL).

The background features a light gray gradient with several realistic water droplets of varying sizes scattered in the corners. The droplets have highlights and shadows, giving them a three-dimensional appearance.

CLASSIFICATION OF ANTIBIOTICS AGENTS ACCORDING TO SITE OF MECHANISM OF ACTION



Cidal or static???

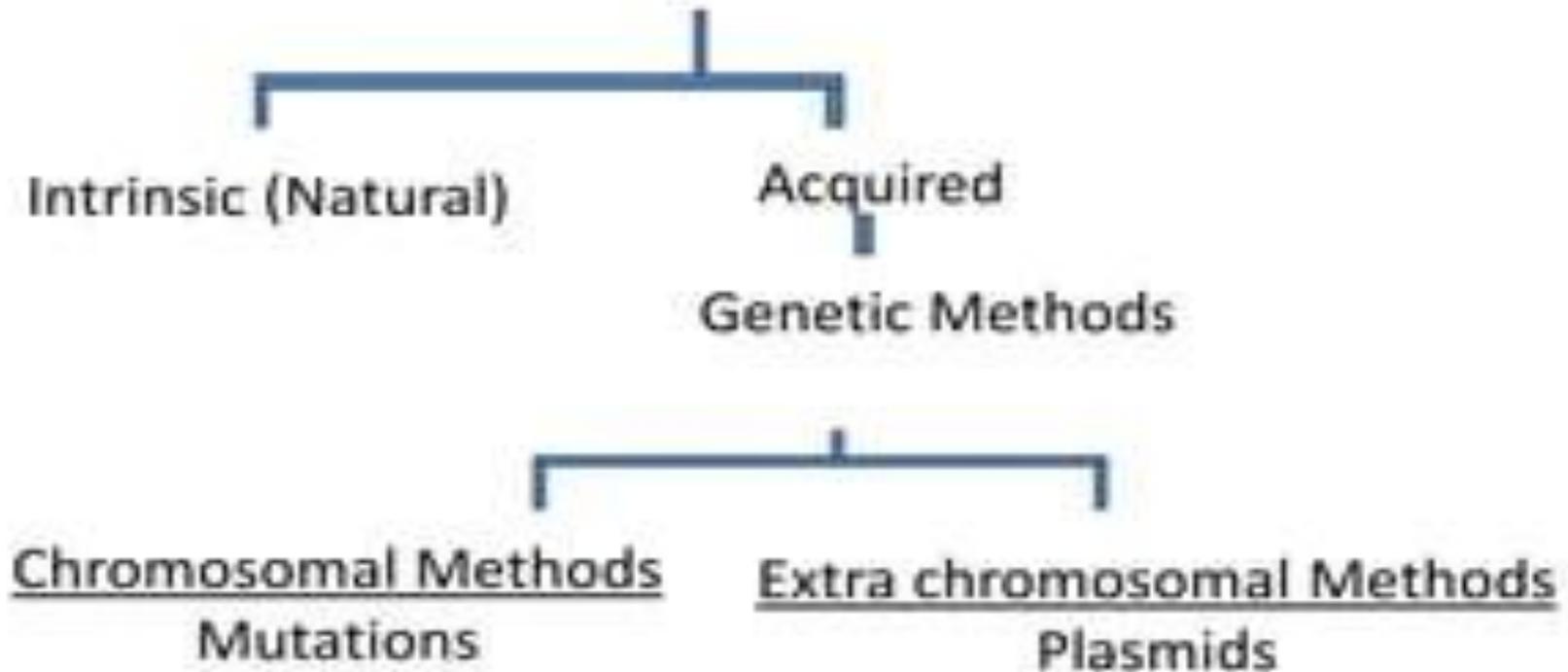
ANTIMICROBIAL RESISTANCE

- THE ABILITY OF A MICROBE (GERM) TO RESIST THE EFFECTS OF A DRUG.
- ANTIMICROBIAL RESISTANCE INCLUDES ANTIBACTERIAL, ANTIFUNGAL, AND ANTIVIRAL RESISTANCE.
- DRUG RESISTANCE MAY BE PRESENT BEFORE TREATMENT IS GIVEN OR MAY OCCUR DURING OR AFTER TREATMENT WITH THE DRUG.

CAUSES OF THE ANTIBIOTIC RESISTANCE

- 1- OVERUSE
- 2- ANTIBIOTICS ARE UNREGULATED AND AVAILABLE OVER THE COUNTER WITHOUT A PRESCRIPTION
- 3- INCORRECTLY PRESCRIBED ANTIBIOTICS
- 4- EXTENSIVE AGRICULTURAL USE
- 5- AVAILABILITY OF FEW NEW ANTIBIOTICS

Mechanism Antibiotic Resistance

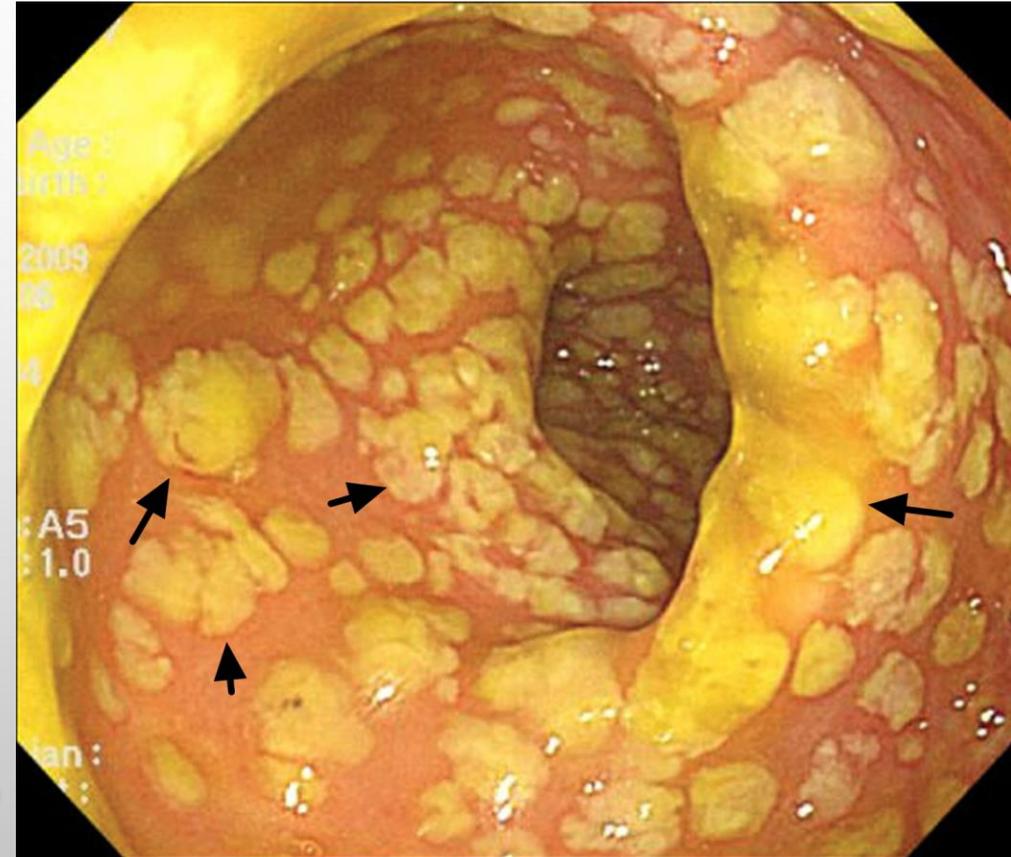


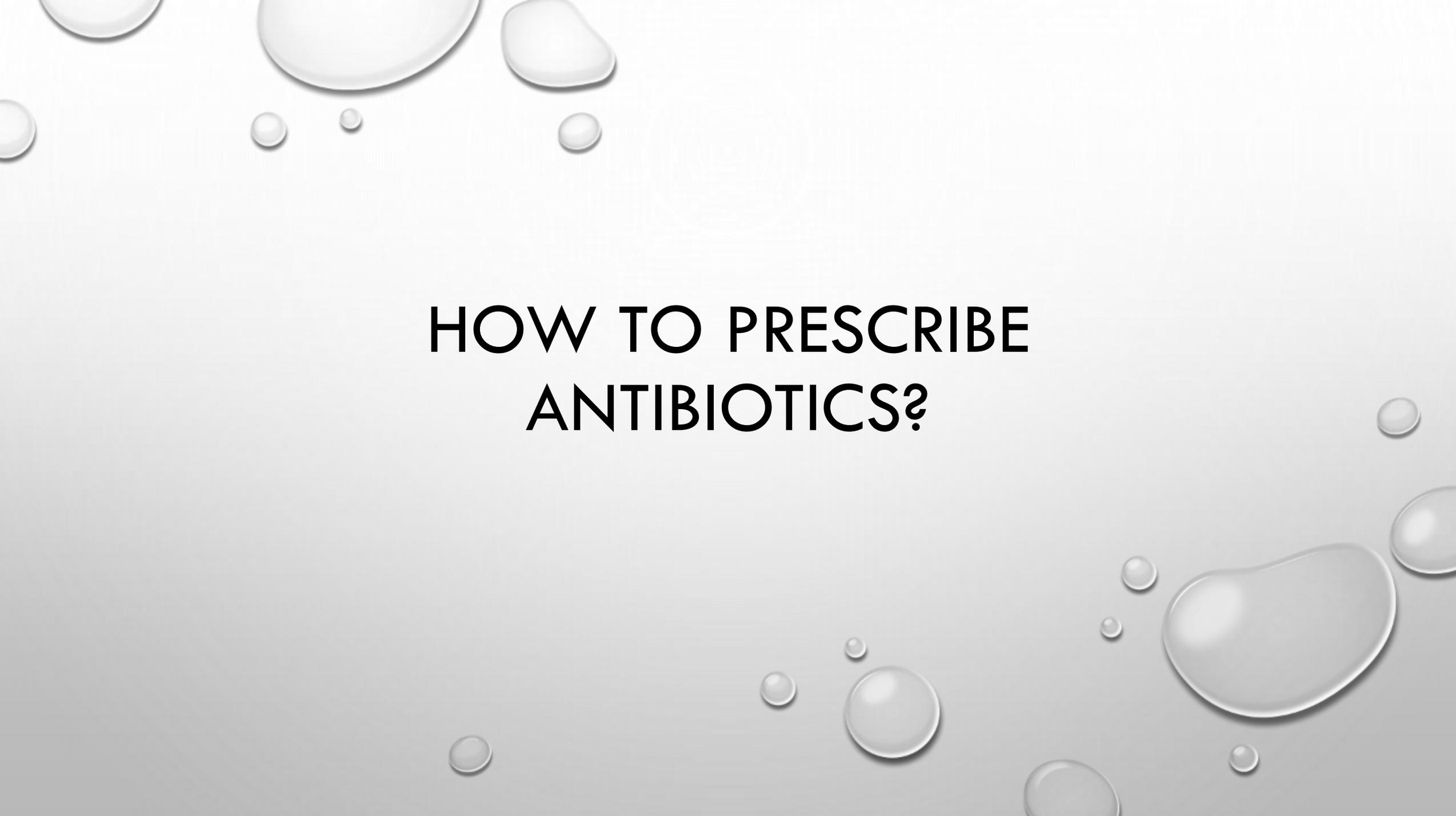
MECHANISMS OF ANTIBIOTIC RESISTANCE

- ANTIBIOTIC RESISTANCE MECHANISMS FALL INTO FOUR MAIN CATEGORIES:
- **(1) LIMITING UPTAKE OF A DRUG**
- **(2) MODIFYING A DRUG TARGET**
- **(3) INACTIVATING A DRUG**
- **(4) ACTIVE DRUG EFFLUX**

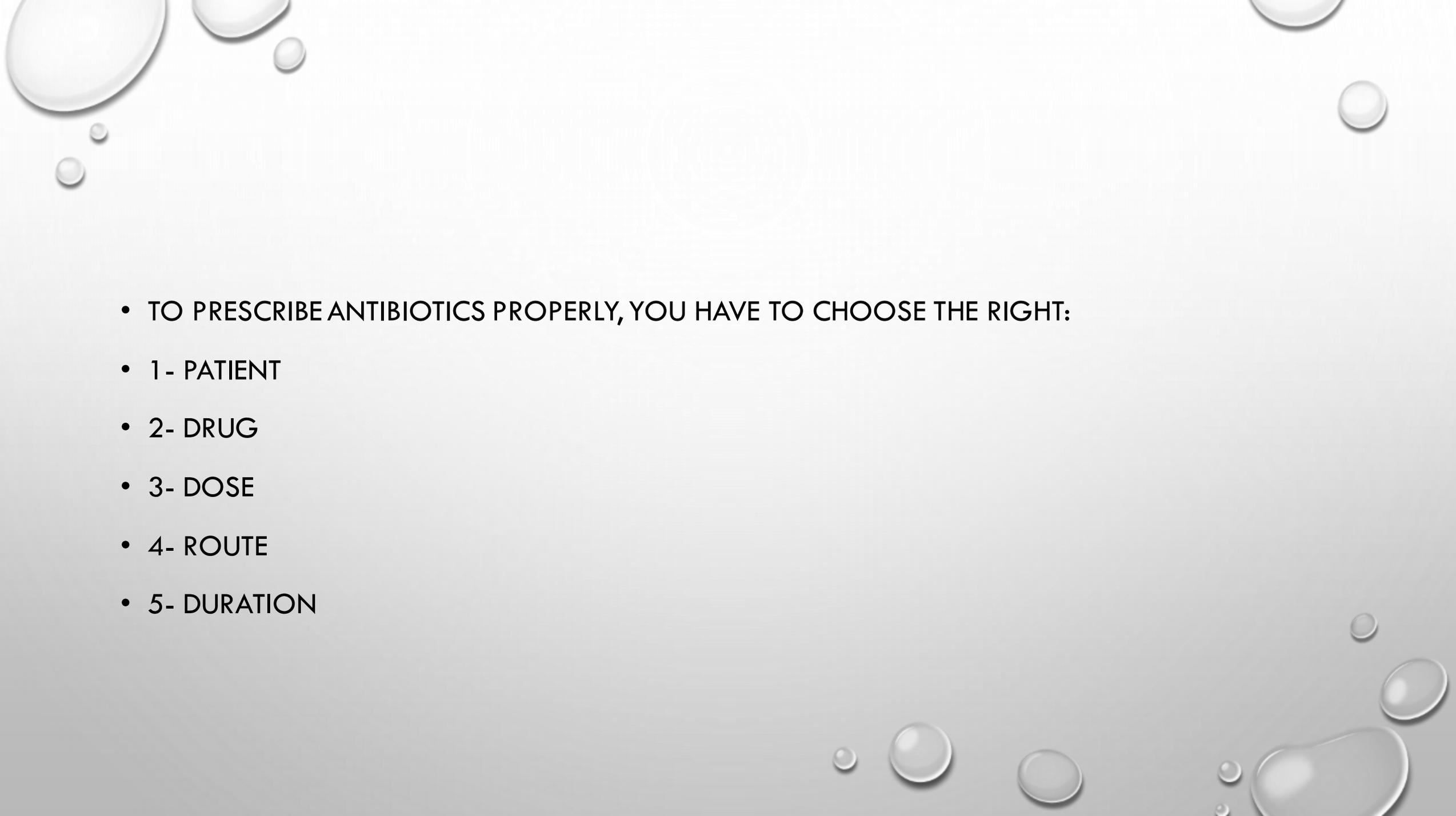
GENERAL SIDE EFFECTS OF ANTIBIOTICS

- 1- ALLERGY
- 2- VITAMIN DEFICIENCY : K & B
- 3- SUPERINFECTION:
- PSEUDOMEMBRANOUS COLITIS: CLOSTRIDIUM DIFFICILE
- CANDIDA INFECTION: THRUSH, PHARYNGITIS



The background of the slide is a light gray gradient with several realistic water droplets of various sizes scattered across it. The droplets have highlights and shadows, giving them a three-dimensional appearance. The text is centered in the middle of the slide.

HOW TO PRESCRIBE ANTIBIOTICS?

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- TO PRESCRIBE ANTIBIOTICS PROPERLY, YOU HAVE TO CHOOSE THE RIGHT:
 - 1- PATIENT
 - 2- DRUG
 - 3- DOSE
 - 4- ROUTE
 - 5- DURATION

1 - THE RIGHT PATIENT

- **CONFIRM BACTERIAL INFECTION BY:**
- 1- FEVER: BODY TEMPERATURE MORE THAN 37.2 C
- 2- CBC: DIFFERENTIAL WBCS COUNT: NEUTROPHILIA INDICATES BACTERIAL INFECTION
- 3- SPECIFIC TESTS: EXAMPLE: WIDAL TEST FOR TYPHOID FEVER

2- THE RIGHT DRUG

- SELECTION OF ANTIBIOTIC IS BASED ON:

• 1- THE CAUSATIVE ORGANISM 2- THE AFFECTED PATIENT 3- TISSUE PENETRATION

- **CAUSATIVE ORGANISM:**

- CULTURE AND SENSITIVITY OF INFECTED MATERIAL: E.G. SPUTUM, URINE, CSF IN MILD AND MODERATE CASES

- START EMPIRICAL ANTIBIOTIC THERAPY IN:

- ACUTELY-ILL PATIENTS, IMMUNOCOMPROMISED, MENINGITIS

- **AFFECTED PATIENT:** FACTORS AFFECTING ANTIBIOTIC CHOICE: AGE, IMMUNE STATE, PREGNANCY

- **TISSUE PENETRATION:**

- CHRONIC PUS FORMATION REQUIRES IV ANTIBIOTIC ADMINISTRATION

- DIABETIC FOOT: ISCHEMIA DELAYS ANTIBIOTIC EFFECT

- BODY BARRIERS: BBB, VITREOUS HUMOR, PROSTATIC BARRIER

3- THE RIGHT DOSE

- MIC: THE LOWEST CONCENTRATION (IN MG/ML) OF AN ANTIBIOTIC THAT INHIBITS THE GROWTH OF A GIVEN STRAIN OF BACTERIA

post-antibiotic effect

- **The post antibiotic effect is the phenomenon of continued bacterial killing even though serum concentrations have fallen below the minimum inhibitory concentration (MIC).**

Patterns of Microbial Killing

■ Concentration dependent

- Higher concentration \longrightarrow greater killing
 - Aminoglycosides, Flouoroquinolones, Ketolides, metronidazole, Ampho B.

■ Time-dependent killing

- Minimal concentration-dependent killing (4x MIC)
- More exposure \longrightarrow more killing
 - Beta lactams, glycopeptides, clindamycin, macrolides, tetracyclines, bactrim

4- THE RIGHT ROUTE

- ACCORDING TO THE SEVERITY OF INFECTION:
- MILD- MODERATE CASES: ORAL
- SEVER CASES:PARENTRAL

5- THE RIGHT DURATION

- ACCORDING TO THE UNIVERSAL GUIDELINES FOR EACH CASE:
- TONSILLITIS: 3-5 DAYS
- UTIS: 10 DAYS
- PNEUMONIA: 7 DAYS
- MENINGITIS: 15 DAYS
- AFTER DISAPPEARANCE OF SYMPTOMS, ANTIBIOTIC SHOULD BE CONTINUED FOR 48-72HS???

ANTIBIOTIC COMBINATIONS

- **INDICATIONS:**

- 1- MIXED INFECTIONS: DIABETIC FOOT, PERITONITIS
- 2- SEVER INFECTION: MENINGITIS
- 3- HIGHLY RESISTANT BACTERIAL STRAINS: TB, PSEUDOMONAS

- **GOOD ANTIBIOTIC COMBINATIONS:**

- 1- SYNERGISM (COMPLEMENTARY): PENICILLIN AND AMINOGLYCOSIDES, PENICILLIN AND SULPHADIAZINE
- 2- ADDITION: TETRACYCLINE AND ERYTHROMYCIN
- **WHAT ABOUT THIS COMBINATION: PENICILLIN AND TETRACYCLINE???**

The background is a light gray gradient with several realistic water droplets of various sizes scattered in the corners. A faint, circular watermark logo is visible in the upper center.

THANK YOU