BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biomedical Science

Course Title : Microbiology

Course Code : BM24AC4

Unit-II

Antimicrobial Chemotherapy

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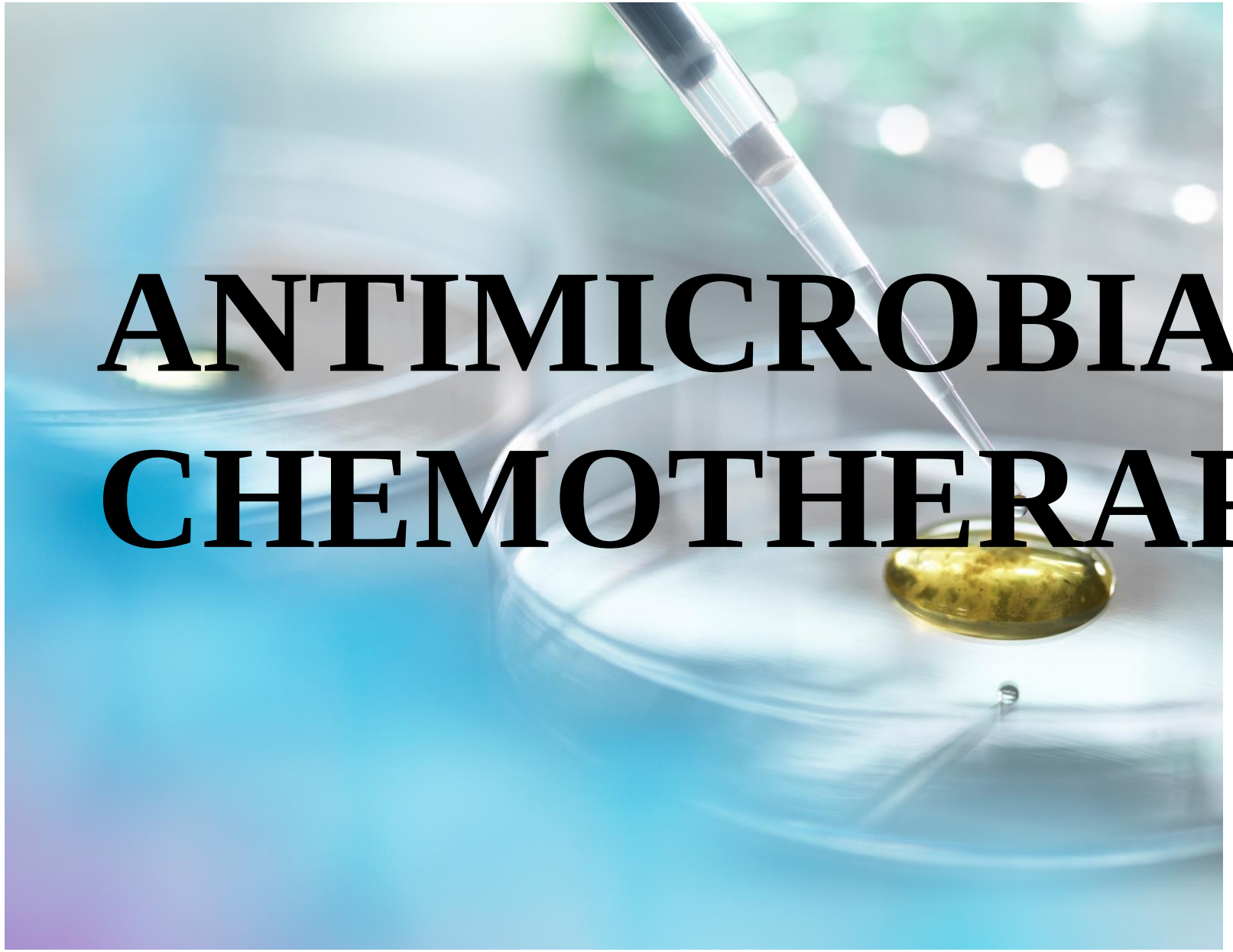


ANTIMICROBIAL CHEMOTHERAPY

CHEMOTHERAPY

Chemotherapy is defined as,

"Treatment of disease by means of chemicals that have a specific toxic effect upon the disease producing microorganisms or that selectively destroy cancerous tissue".

According to American Cancer Society 'the use of medicines or drugs to treat cancer."

CHEMOTHERAPEUTIC AGENTS

1. Alkylating Agents
2. Anti- tumor Antibiotics
3. Antimetabolitics
4. Antimicrotubule Agents

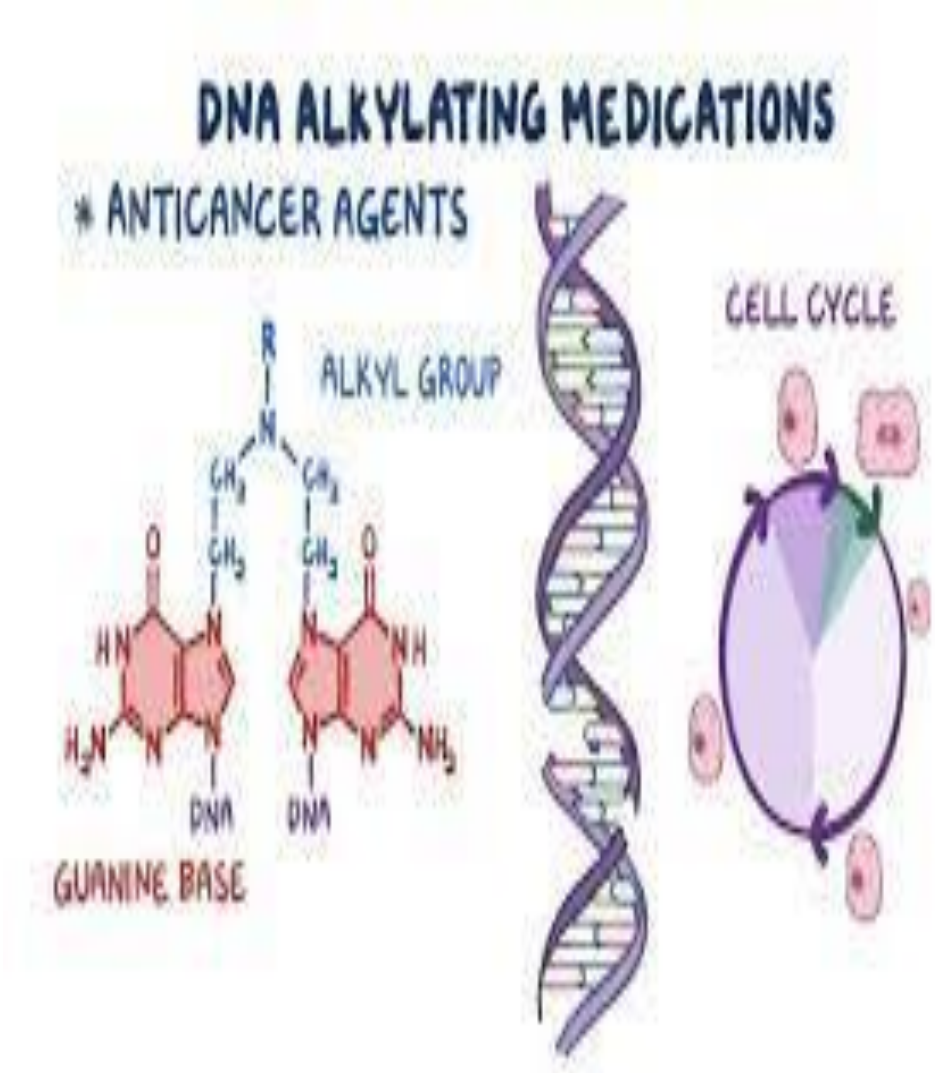
1.ALKYLATING AGENT

Mode Of Action :

Arrests DNA replication can result in DNA damage.

Example :

- Carmustine
- Mustine



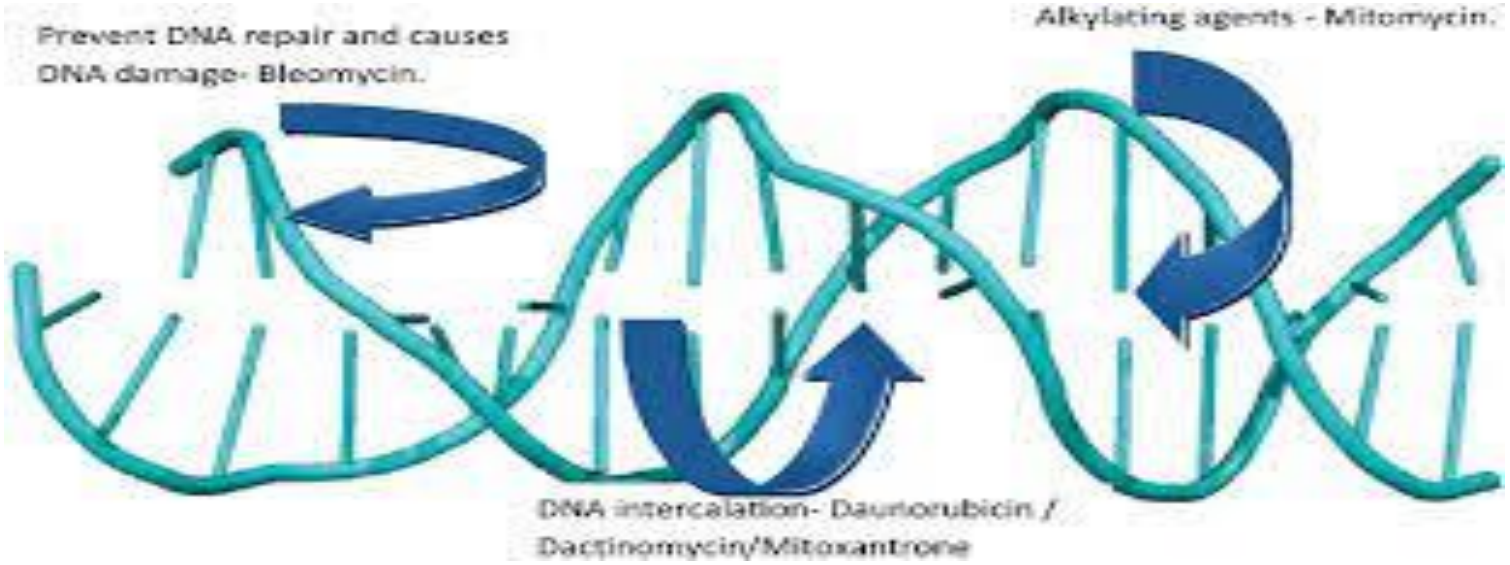
2.ANTI- TUMOR ANTIBIOTICS

Mode Of Action :

Alter the DNA inside cancer cells to keep them from growing and multiplying.

Example :

- Daunorubicin
- Actinomycin D



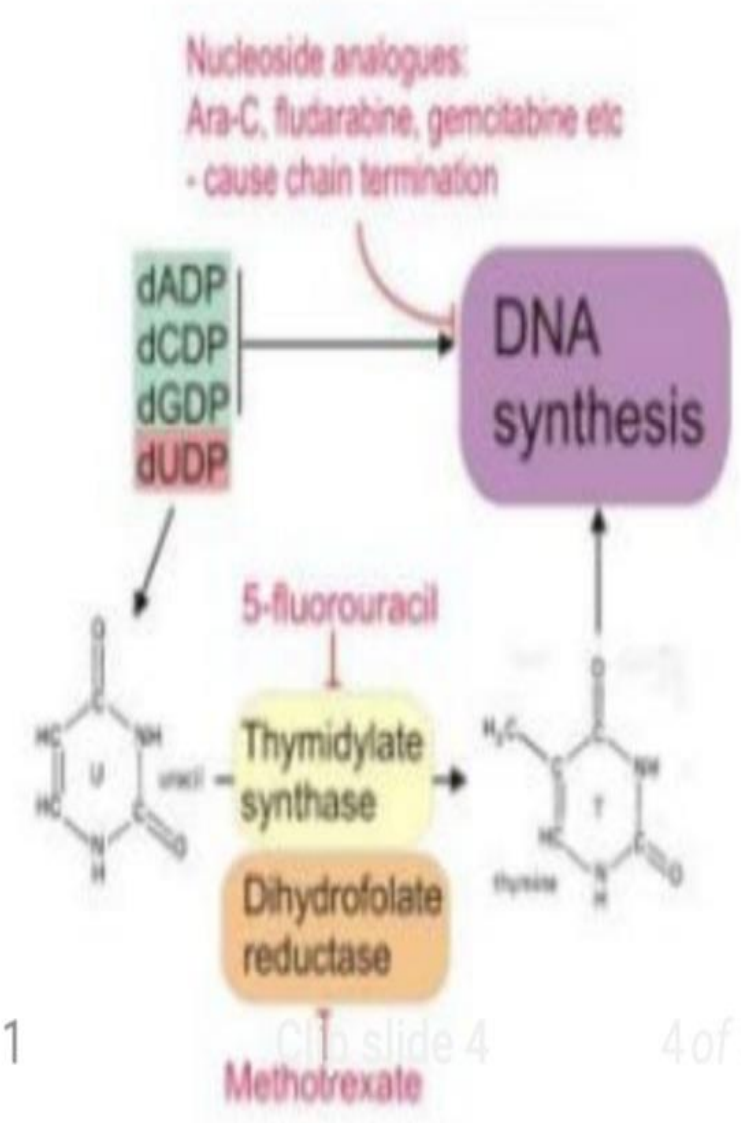
3.ANTIMETABOLITICS

Mode Of Action :

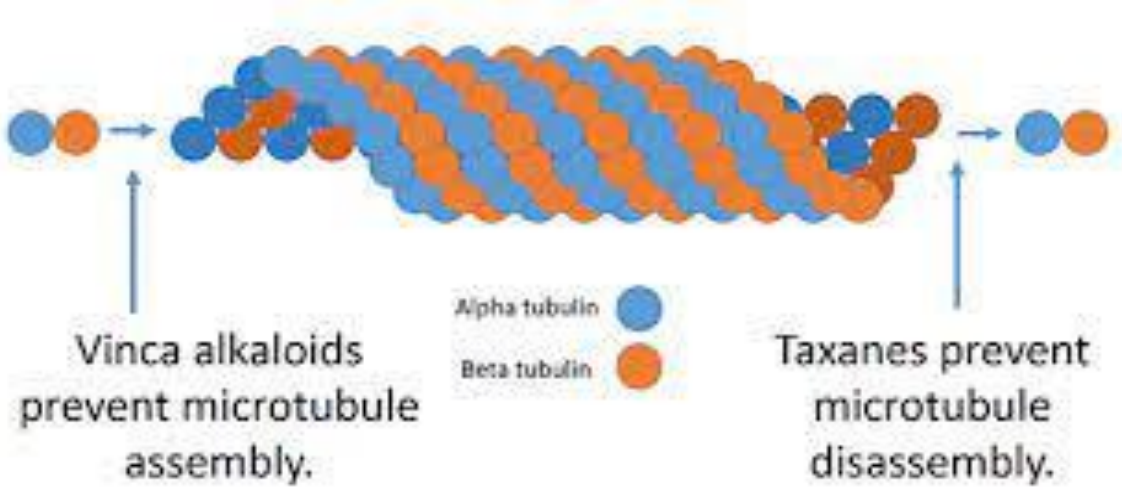
Interfere with the availability of normal purine or pyrimidine nucleotide precursors either by inhibiting their synthesis or by competing with them in DNA or RNA synthesis.

Examples :

- Methotrexate
- 5-FU



4.Antimicrotubule Agents



Mode Of Action:

Block cell division by preventing microtubule function.

Example :

- Vinca alkaloids prevent the formation of the microtubules.
- Taxanes prevent the microtubule disassembly.

DEFINITION OF ANTIMICROBIAL CHEMOTHERAPY

- Antimicrobial chemotherapy involves the administration of drugs with selective toxicity against pathogens involved not host cells.
- Antibiotics which are agents used to combat bacteria are among the most common antimicrobials.

HISTORY

- The father of antimicrobial chemotherapy is Paul Ehrlich.
- Paul Ehrlich in Germany developed first antimicrobial compound salvarsan against syphilis in 1910 .
- Alexander Fleming discovered penicillin in 1928 a break through in history of medicine.

- When I woke just after down on September 28 1928 I certainly didn’t plan to revolutions all medicine by discovering the world’s first antibiotic.
- In 1935 German biochemist Gerhard Domagk developed the first sulfonamides a synthetic and the first commercially available drug in name of prontosil.

PRINCIPLE OF ANTIMICROBIAL CHEMOTHERAPY

SELECTIVE TOXICITY :

- Antimicrobials are based on concept of selective toxicity.
- Ability of a drug to injure a target cell or organism without other cells or organisms that are in intimate contact.

REASONS OF SELECTIVE TOXICITY :

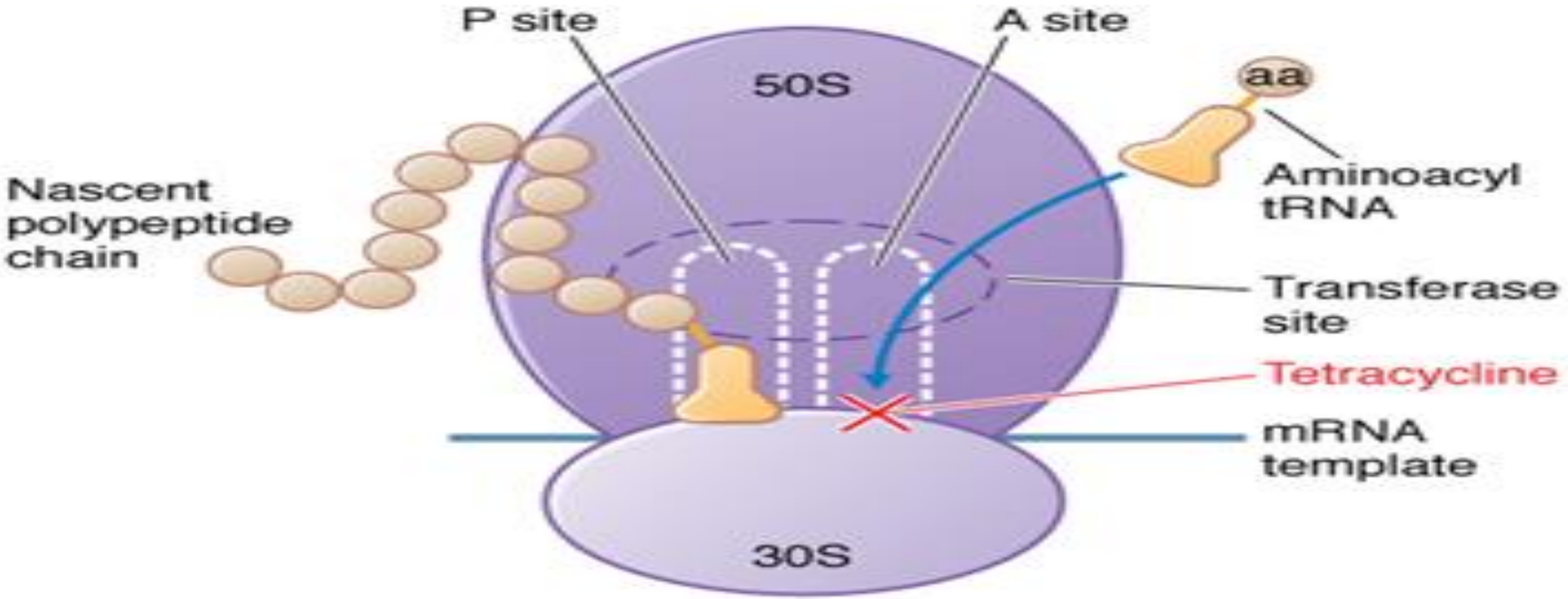
1.Drug accumulates in microbe more than in human cells.

2. Drug is targeted against particular feature of microbe not present in host.

Examples :

- Penicillin inhibits peptidoglycan synthesis in the cell wall nor peptidoglycan.
- Streptomycin target bacterial protein synthesis because bacterial ribosomes (70s) are different from ribosomes (80s) of human and other eukaryotic organisms.

TETRACYCLINE IS USED TO TREAT ACNE AND CHOLERA



TYPES OF ANTIMICROBIAL CHEMOTHERAPY

1.Antibacterial Chemotherapy

2. Antifungal Chemotherapy

3. Antiprotozoal Chemotherapy

4. Antiviral Chemotherapy

1.ANTIBACTERIAL CHEMOTHERAPY :

- Used to treat bacterial infections e.g tuberculosis.
- **Broad Spectrum Antimicrobial** are active against both gram +ve and –ve.

Example :

Tetracyclines

Phenicol

- **Narrow Spectrum Antibacterial** have limited activity and are only useful against particular species.
- For example glycopeptides and bacitracin are only effective against gram –ve bacteria.

Example :

Penicillin

Aminoglycosides

Erythromycin

2.ANTI VIRAL CHEMOTHERAPHY

To stop development of virus in host e.g HIV influenza , Herpes simplex.

Example :

Acyclovir

Amantadine B

Zidovudine

3.ANTIFUNGAL CHEMOTHERAPY :

To treat fungal infections such as athlete’s foot, ringworm , candidiasis (thrush) , serious cryptococcal meningitis.

Example

Amphotericin B

Ketoconazole

Griseofulvin

4.ANTIPROZOAL CHEMOTHRAPY

To kill single cell infective protozoans like Entamoeba histolytica (ulcer of intestines) plasmodium (malaria) Trypanosoma brucei (sleeping sickness).

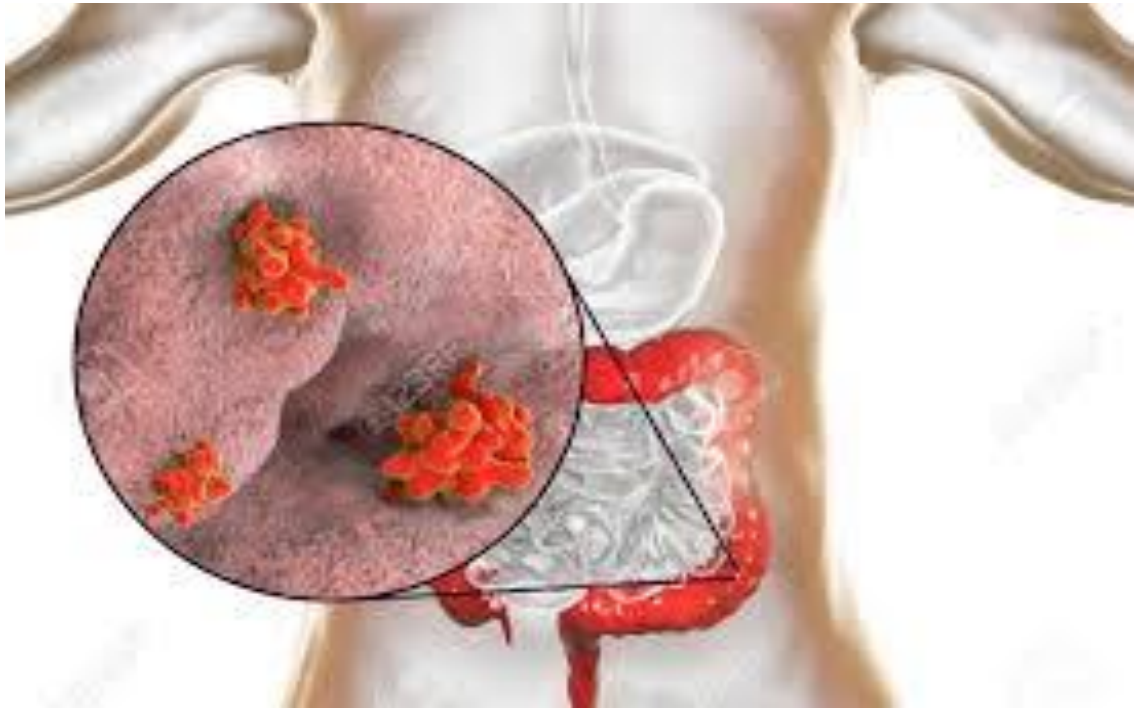
Example :

Chloroquine

Pyrimethamine

Tinidazole

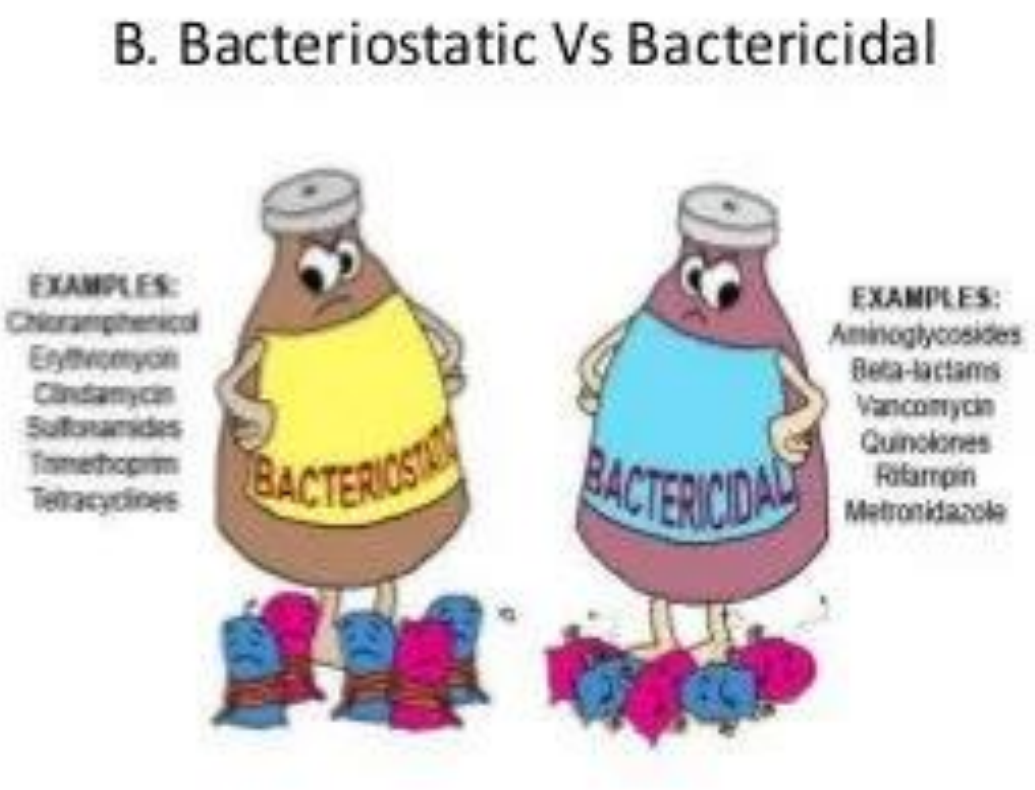
Nifursemizone



TYPES OF ACTION

1.Bacteriostatic

2.Batericidal



1.BACTERIOSTATIC :

Inhibit the growth of bacteria.

Example :

- Sulfonamides
- Tetracyclines
- Chloramphenicol
- Erythromycin
- Ethambutol

2. Bactericidal :

Kill the microbes

Example :

- Penicillin
- Aminoglycosides
- Polypeptide
- Rifampin
- Isoniazid , Vancomycin
- Metronidazole , Cotrimoxazole

MECHANISM OF ACTION

Thus the mechanism of action of a chemotherapeutic depend on the inhibition of a metabolic channel or a structure that is present in the microbe but not in the host cell several mechanisms are known,

1. Inhibition of cell wall synthesis
2. Inhibition of protein synthesis
3. Alteration of cell membranes
4. Inhibition of nucleic acid synthesis
5. Antimetabolite activity

Cell Wall Synthesis

Beta Lactams
Penicillins
Cephalosporins
Carbapenems
Monobactams

Vancomycin
Bacitracin

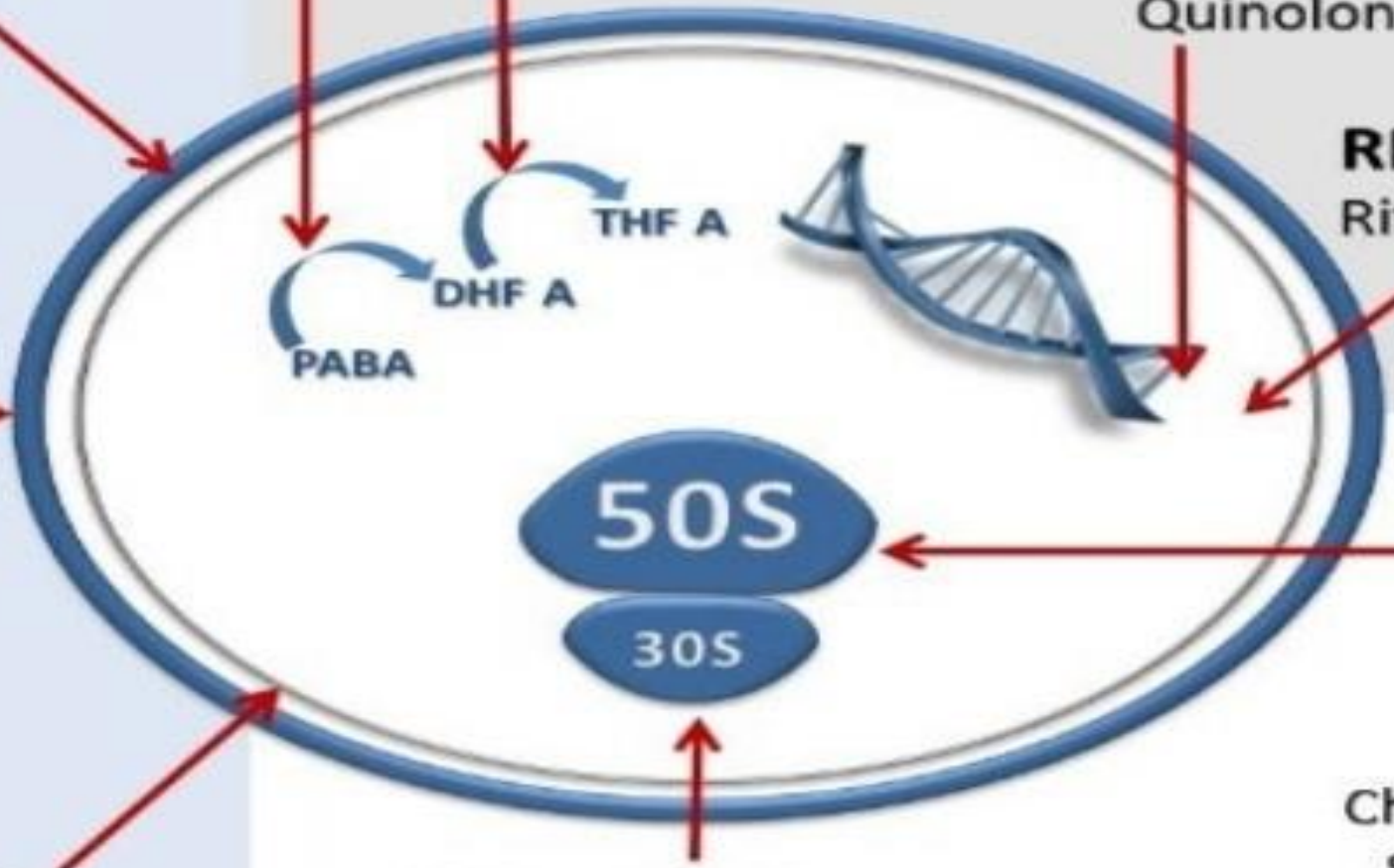
Cell Membrane
Polymyxins

Nucleic Acid Synthesis

Folate synthesis
Sulfonamides
Trimethoprim

DNA Gyrase
Quinolones

RNA Polymerase
Rifampin



50S subunit
Macrolides
Clindamycin
Linezolid
Chloramphenicol
Streptogramins

30S subunit
Tetracyclines
Aminoglycosides

Protein Synthesis

1.INHIBITION OF CELL WALL SYNTHESIS :

- Due to its unique structure and function the bacterial cell wall is an ideal point of attack by selective toxic agents.
- Some antibiotics penicillin, vancomycin , bacitracin interfere with cell wall synthesis and cause bacteriolysis.

2.INHIBITION OF PROTEIN SYNTHESIS :

- Many antimicrobial chemotherapeutics block protein synthesis by acting on the 30s or 50s subunits if the bacterial ribosomes.
- Examples are chloramphenicol, tetracycline, erythromycin and the aminoglycosides.

Example :

1. Aminoglycosides
2. Tetracyclines
3. Chloramphenicol
4. Macrolides

3.ALTERATION OF CELL MEMBRANES :

- Some antibiotics cause disruption of the cytoplasmic membrane and leakage of cellular proteins nucleotides leading to cell death .

Example :

Polymyxins, amphotericin B and nystatin are examples.

4. INHIBITION OF NUCLEIC ACID SYNTHESIS :

- These can act on any steps of DNA or RNA replications.
- DNA – Quinolones , Metronidazole.
- RNA – Rifampin , Bacitracin.

5. Antimetabolite activity :

- In which the chemotherapeutic agent competes with an essential metabolite for the same enzymes e.g p-aminobenzoic acid (PABA) is an essential metabolite for many organisms .
- They use it as a precursor in folic acid synthesis. Which is essential for nucleic acid synthesis. Sulphonamides are structural analogue to PABA so they enter into the reaction in place of PAPA and complete for the active center of the enzyme thus inhibiting folic acid synthesis.

Example :

Sulphonamides

SOURCES OF ANTIMICROBIAL CHEMOTHERAPY

- Plants (herbs and spices , fruits and vegetables, seeds and leaves) are the main source of antimicrobials and contain many essential oils that have preservation effect against different microorganisms.
- Synthetic drugs (e.g Sulphonamides)
- Antibiotics (e.g Penicillin)
- In practice synthetic drugs often referred to antibiotics synthetic drugs.
- Laboratory synthesized molecules e.g sulphonamides antibiotic.

- **Natural Products** : Produced by one microorganism & inhibit the growth of kill second microorganism at low conc.
- Non – synthetic chemotherapeutic agent produced by microorganisms isolated & purified for human use. e.g Penicillin.

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Thank You