# GENERAL PRINCIPLES OF CHEMOTHERAPY

This type of therapy is generally called chemotherapy which has come to mean 'treatment of systemic infections with specific drugs that selectively suppress the infecting microorganism without significantly affecting the host.' The basis of selective microbial toxicity is the action of the drug on a component of the microbe (e.g. bacterial cell wall) or metabolic processes (e.g. folate svnthesis) that is not found in the host, or high affinity for certain microbial biomolecules (e.g. trimethoprim for bacterial dihydrofolate reductase). Due to analogy between the malignant cell and the pathogenic microbes, treatment of neoplastic diseases with drugs is also called 'chemotherapy'.

**Anti biotics** These are substances produced by microorganisms, which selectively suppress the growth of or kill other microorganisms at very low concentrations.

**Antimicrobial agent** (AMA) to designate synthetic as well as naturally obtained drugs that attenuate microorganisms.

**CLASSIFICATION**

Antimicrobial drugs can be classified in many ways:

A. Chemical structure

1. Sulfonamides and related drugs: Sulfadiazine and others, Sulfones-Dapsone (DDS), Paraaminosalicylic acid (PAS) .

2. Oiaminopyrimidines: Trimethoprim, Pyrimethamine.

3. Quinalones: Nalidixic acid, Norfloxacin,Ciprofloxacin, Gatifloxacin, etc.

4. -Lactam antibiotics: Penicillins, Cephalosporins, Monobactams, Carbapenems.

5. Tetracyclines: Oxytetracycline, Doxycycline,etc.

6. Nitrobenzene derivative: Chloramphenico:

?. Aminog/ycosides: Streptomycin, Gentamycin,Amikacin, Neomycin, etc.

8. Macrolide antibiotics: Erythromycin, Clanthromycin,Azithromycin, etc.

9. Lincosamide antibiotics: Lincomycin, Clindamycin.

10. Glycopeptide antibiotics: Vancomycir Teicoplanin.

11. Oxazolidinone: Linezolid.

1 2. Polypeptide antibiotics: Polymyxin-B, Coltin,Bacitracin, Tyrothricin.

13. Nitroimidazoles: Metronidazole, Tinidazole etc.

1 5. Nicotinic acid derivatives: Isoniazid, Pyrczinamide,Ethionamide.

16. Polyene antibiotics. Nystatin, Amphotericin-B, Hamycin.

17. Azote derivatives:Miconazole, Clotrimoxzole, Ketoconazole, Fluconazole.

18. Others: Rifampin, Spectinomycin, Cycloserine, Viomycin, Ethambutol, Thiacetazone, Clofazimine, Griseofulvin.

B. Mechanism of action

1. Inhibit cell wall synthesis: Penicillin, Cephalosporins, Cycloserine, Vancomycin, Bacitracin.

2. Cause leakage from cell membranes: Poly-peptides-Polymyxins, Colistin, Bacitracin, Polyenes-Amphotericin B, Nystatin, Hamycin.

3. Inhibit protein synthesis: Tetracycline, Chloramphenicol, Erythromycin, Clindamycin, Linezolid.

4. Cause misreading ofm-RNA code and affect permeability: Aminoglycosides-Streptomycin, Gentamicin, etc.

Inhibit DNA gyrase: Fluoroquinolones Ciprofloxacin and others.

Interfere with DNA function: Rifampin, Metronidazole.

- Interfere with DNA synthesis: Acyclovir, Zidovudine.

- Interfere with intermediary metabolism: Sulfonamides, Sulfones, PAS, Trimethoprim, Pyrimethamine, Ethambutol.

C.Type of organisms against which primarily active

1. Antibacterial: Penicillins, Aminoglycosides, Erythromycin, etc.

2. Antifungal: Griseofulvin, Amphotericin B,

Ketoconazole, etc.

3. Antiviral: Acyclovir, Amantadine, Zidovudine,

etc.

4. Antiprotozoal: Chloroquine, Pyrimethamine, Metronidazole, Diloxanide, etc.

5. Anthelmintic: Mebendazole, Pyrantel, Niclosamide, Diethyl carbamazine, etc.

D. Spectrum of activity

Narrow-spectrum

Penicillin G, streptomycin

Broad-spectrum Tetracyclines Chloramphenicol Hypersensitivity reactions

Practically all AMAs are capable of causing hypersensitivity reactions. These are unpredictable and unrelated to dose. The whole range of reactions from rashes to anaphylactic shock can beproduced. The more commonly involved AMAs are-penicillins, cephalosporins, sulfonamides,fluoroquinolones.

**Drug resistance**

It refers to unresponsiveness of a microorganismto an AMA, and is akin to the phenomenon oftolerance seen in higher organisms.

**Natural resistance** Some microbes have always been resistant to certain AMAs. They lack themetabolic process or the target site which is affected by the particular drug.

**Acquired resistance** It is the development of resistance by an organism (which was sensitivebefore) due to the use of an AMA over a period of time.

**Superinfection (Suprainfection) infection occurring after or on top of an earlier infection, especially following treatment with broad-spectrum antibiotics** This refers to the appearance of a new infection as a result of antimicrobial therapy.

Use of most AMAs causes some alteration o f the normal microbial flora of the body. The normal flora contributes to host defence elaborating substances called bacteriocins which inhibit pathogenic organisms. Further pathogen has to compete with the normal flora for nutrients, etc. to establish itself

Superinfections are more common when the defence is compromised.

- Corticosteroid therapy
- Leukaemias and other malignancies, especially when treated with anticancer drugs
- Acquired immunodeficiency syndrome (AIDS
- Agranulocytosis
- Diabetes, disseminated lupus erythematosus