

CHEMOTHERAPY: Introduction

Presented by-

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Chemotherapy

- It may be defined as the treatment of **systemic infection** (caused by bacteria, viruses, fungi, protozoa, helminths etc.) **or malignancy** with **specific chemicals** that have *selective toxicity* for infecting organism /malignant cell with no or minimal effect on the host cell.
- Drug: Pharmacotherapeutic Agent + Chemotherapeutic Agent

- The Chemotherapeutic agents have minimal or negligible effect on the host
- The basis of selective toxicity is variation in structural component and or metabolic processes between the host cell and pathogen.
- Most of the antibiotics exhibits a great degree of selectivity such as:-
 - a. Inhibition of bacterial cell wall formation (penicillin's/cephalosporins)
 - b. Inhibition of bacterial protein synthesis(tetracycline, aminoglycosides etc.)
 - c. Bacteriostatic effect of sulphonamides is due to PABA antagonism in folic acid synthesis

Antibiotics

- Antibiotics constitute a large portion of chemotherapeutic agent
- Antibiotics are substances produced **by microorganism(fungi, Actinomycetes or bacteria)**, which selectively suppress the **growth or kill *other* microorganism** at ***very low*** concentration.
- **Antimicrobial Agent**: Are term used to designate synthetic as well as naturally obtained drug that attenuate microorganism

HISTORY

- The work of Ehrlich prompted search for newer chemicals as antibacterial and he was rewarded with Nobel prize in the year 1909.
 - Father of chemotherapy:- Paul Ehrlich.
 - German Gerhard Domagk discovered antibacterial activity of another dye prontosil.
 - Domagk was also honoured with the Nobel prize in medicine (1938).
 - Pasteur and Joubert ,who showed bacterial property of common bacteria against anthrax bacilli, first demonstrated the phenomenon of antibiosis b/w microorganisms.
- Penicillin was discovered in (1941). treating with human bacterial infection.

- Alexander Fleming in (1928) working at penicillium notatum prevented the bacteria. it was established as an antibiotic by Florey and Chain and his associates in treating wounded soldiers during world war II.
- Fleming Florey and Chain were awarded Nobel prize in (1945).
- Streptomycin was isolated from Streptomyces griseus by Waksman in (1945).
- Antibiotics were discovered viz:-
 - Chloramphenicol- 1947
 - Amphotericin B- 1956
 - Cephalosporins – 1960
 - Gentamycin- 1964
 - Fluroquinolones- 1980

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Antimicrobial Agents

➤ These **are synthetic** as well as **naturally obtained** (microbial origin) drug that are used to inhibit or kill micro-organisms.

➤ **Classification of AMAs**

a) **Based on antibacterial action:-**

Bacteriostatic :- Suppression of bacterial growth and multiplication.

Eg.- Sulphonamides, tetracyclines, erythromycin, chloramphenicol.

Bactericidal :- Cause death of bacteria.

Eg.- Penicillin ,cephalosporins, streptomycin, kanamycin, colistin, bacitracin etc

b) Based on Antibacterial spectrum:-

Narrow Spectrum :- Effective against a limited group of bacteria.

- i) Gram positive :- Penicillin G, erythromycin, lincomycin, bacitracin etc.
- ii) Gram negative:- Streptomycin, gentamycin, polymyxinB etc.

Broad spectrum :- Effective against both Gram positive & Gram negative bacteria E.g.:- Tetracyclines, chloramphenicol, fluoroquinolones, Sulfonamide

Note: Drugs with all range of intermediate band width are now available

Based on Mechanism of antimicrobial action

I. By inhibiting bacterial cell wall formation or causing its break down leading to death of the microbes.

E.g.:- (Penicillins, cephalosporins, bacitracin, vancomycin).

ii). By altering microbial cell membrane permeability causing leakage of essential intracellular components:-

E.g.:- Polyene antifungal antibiotics (nystatin & amphotericin B) exert antifungal action by binding to ergosterol of fungal cell membrane, acting as ionophores causes leakage of cations (K) from the fungal cell.

iii). By inhibiting synthesis of ergosterol in cell membrane of fungi:- antifungal drug itraconazole.

iv). By disrupting the structural integrity of bacterial cell membrane :- The cationic detergent antibiotics polymyxin B, & colistin interact with bacterial cell membrane and disrupt its structure causing bactericidal effect.

v) **By interfering with protein synthesis in bacteria e.g.,** Tetracyclines, chloramphenicol, Erythromycin, clindamycin, linezolid

vi) **By causing misreading of mRNA code and affect permeability**

e.g.:- Aminoglycosides.

vii) By interfering with nucleic acid synthesis by the following mechanism :-

a.) By inhibiting nucleic acid synthesis (DNA & RNA):-

Sulphonamides and sulfones, pyrimethamine Acyclovir, Zidovudine

b.) By altering base pairing properties of the template :- Proflavine and acriflavine cause frame shift mutation altering the codons for synthesis of a new protein instead of the normal protein in bacteria.

c.) Inhibition of either DNA or RNA polymerase in bacteria :-

Rifamycin and rifampicin (antiTB antibiotics) inhibit bacterial RNA polymerase. Ciprofloxacin and Norfloxacin inhibit DNA gyrase

Based on sources

- a. Fungal Origin:-** penicillin ,Cephalosporin and Griseofulvin.
- b. Bacterial Origin:-** Bacitracin , Polymyxin B,Colistin ,tyrothricin.
- c. Actinomycetes Origin:-** Streptomycin, tetracyclines, chloramphenicol, Macrolides

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Principle of chemotherapy

- a. The basic principle of chemotherapy is the selective toxicity i,e the drug should selectively inhibit or kill the disease causing pathogenic organism .
- b. Chemotherapy must be rational and needs to be supported by either a clinical or microbiological diagnosis to identify the pathogenic organisms.
- c. Characterization of the pathogens including its sensitivity to an AMAs is essential.

- a. Selection of an appropriate drug based on pathogenic organism, patient factors and drug factors.
- b. The drug should be used in proper time, by proper route ,at appropriate dose rate and for a proper duration.
- c. Attainment of effective concentration of a chemotherapeutic agent for a sufficient period at the site of infection (tissue or body fluid) is very important.
- d. Specific and appropriate supportive therapy should be undertaken to overcome the infection.

THANK YOU

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