

Chemotherapy

Introduction to Chemotherapy

Definition of Chemotherapy:

- Chemotherapy, in its broadest sense, refers to the treatment of diseases using chemical substances.
- However, in the context of infectious diseases and cancer, chemotherapy refers specifically to the use of chemicals (chemotherapeutic agents) to kill or inhibit the growth of infectious organisms or malignant cells without causing significant damage to the host's normal tissues.

History of Chemotherapy:

- The foundations of modern chemotherapy were laid by Paul Ehrlich, who coined the term "magic bullet" and developed Salvarsan for syphilis.
- Later, Alexander Fleming's discovery of penicillin in 1928 marked a revolution in antimicrobial chemotherapy.

Classification of Chemotherapeutic Agents:

1. Antimicrobial Agents:

- Used to treat infections caused by bacteria, viruses, fungi, protozoa, and helminths.
- **Examples:** antibiotics, antivirals, antifungals, antiprotozoals, and anthelmintics.

2. Antineoplastic (anticancer) Agents:

- Used in the treatment of various cancers or neoplasms.

Antimicrobial Chemotherapy:

- Focuses on agents used to kill or inhibit the growth of microorganisms (bacteria, viruses, fungi, protozoa, helminths).

Basic Concepts in Antimicrobial Therapy:

A. Selective Toxicity

- The ideal chemotherapeutic agent should selectively target the pathogen without harming the host.
- This is possible because pathogens possess unique structures and metabolic pathways absent in human cells.
- **Examples:**
 - Bacterial cell wall (peptidoglycan) → Targeted by *penicillin*.
 - Bacterial ribosomes (70S) → Targeted by *tetracyclines*, *aminoglycosides*.
 - Viral enzymes (e.g., reverse transcriptase) → Targeted by *antiretroviral drugs*.

B. Bactericidal vs. Bacteriostatic Drugs

- **Bactericidal:** Kill bacteria directly (e.g., *penicillin*, *aminoglycosides*).
- **Bacteriostatic:** Inhibit bacterial growth, allowing host immunity to eliminate them (e.g., *tetracycline*, *chloramphenicol*).

C. Spectrum of Activity

- **Narrow-spectrum:** Active against specific types of organisms (e.g., *penicillin G* against Gram-positive bacteria).
- **Broad-spectrum:** Active against a wide range of organisms (e.g., *tetracyclines*, *fluoroquinolones*).

D. Minimum Inhibitory Concentration (MIC)

- The lowest concentration of a drug that inhibits visible microbial growth *in vitro*.
- Used to guide dosage and antibiotic selection.

E. Resistance

- Microorganisms can develop resistance through:
 - **Mutation**
 - **Gene transfer** (via plasmids, transposons)
- Types:
 - **Intrinsic resistance:** Natural resistance due to structural or functional characteristics.
 - **Acquired resistance:** Resistance developed through mutation or acquisition of resistance genes.
- Mechanisms of resistance include:
 - Enzymatic degradation (e.g., beta-lactamases),
 - Alteration of drug targets,
 - Increased efflux,
 - Reduced permeability.

Factors Influencing the Efficacy of Chemotherapy:

1. Host Factors:

- Age, renal and hepatic function
- Immune status
- Pregnancy or lactation
- Allergies

2. Pathogen Factors:

- Susceptibility
- Site of infection (e.g., CNS, bone)
- Resistance pattern

3. Pharmacokinetic and Pharmacodynamic Properties of Drug:

- Absorption
- Distribution
- Metabolism
- Excretion
- Concentration at site of infection
- Time vs. concentration-dependent killing

Prophylactic vs. Therapeutic Chemotherapy:

- **Prophylactic (Preventive):** To prevent infection in high-risk situations.
 - Example: Antimalarial drugs for travelers, antibiotics before surgery.
- **Therapeutic:** To treat active infection or malignancy.

Combination Chemotherapy:

- **Used to:**
 - Prevent or delay resistance (e.g., TB treatment).
 - Broaden spectrum.
 - Achieve synergistic effects.

Chemotherapy in Cancer:

- Chemotherapeutic agents target rapidly dividing cells.
- Includes alkylating agents, antimetabolites, mitotic inhibitors, topoisomerase inhibitors, and monoclonal antibodies.
- **Major limitations:**
 - Toxicity to normal dividing cells (e.g., bone marrow, GI tract).
 - Development of resistance.
 - Narrow therapeutic index.



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