

Chemotherapy

Chemotherapy (General Principles in Advanced Pharmacology)

- **Chemotherapy** refers to the use of chemical agents (drugs) to kill or inhibit the growth of microorganisms or cancer cells without causing excessive harm to the host (patient).



- In **antimicrobial chemotherapy** → target bacteria, viruses, fungi, parasites
- In **anticancer chemotherapy** → target rapidly dividing cancer cells

Principles of Cancer Chemotherapy

A. Selective Toxicity

- Drugs aim to kill cancer cells more than normal cells
- Not perfectly selective → causes toxicity

B. Cell Cycle Specificity

- **Some drugs act only during specific phases:**
 - S phase (DNA synthesis): e.g., antimetabolites
 - M phase (mitosis): e.g., vinca alkaloids
- Others act in all phases (non-specific)

C. Growth Fraction

- Tumors with high growth fraction respond better
- Slow-growing tumors are less sensitive

Mechanisms of Action

1. Alkylating Agents

- Add alkyl groups to DNA → cross-linking
- Prevent DNA replication and transcription
- Example: Cyclophosphamide

2. Antimetabolites

- Mimic normal cellular substrates
- Interfere with DNA/RNA synthesis
- Example: Methotrexate (folate antagonist)

3. Topoisomerase Inhibitors

- Prevent DNA unwinding
- Leads to DNA breaks
- Example: Doxorubicin

4. Mitotic Inhibitors

- Disrupt microtubules
- Prevent chromosome separation
- Example: Vincristine

5. Hormonal Therapy

- Block hormone-dependent tumor growth
- Example: Tamoxifen (breast cancer)

Pharmacokinetics

A. Administration

- Mostly IV (due to poor oral bioavailability)
- Some oral agents exist

B. Distribution

- Wide distribution, but limited CNS penetration (except some drugs)

C. Metabolism

- Mainly hepatic
- Some are prodrugs (activated in liver)

D. Elimination

- Renal or biliary
- Dose adjustment needed in organ dysfunction

Combination Chemotherapy

Advantages:

- Broader coverage
- Preventing resistance
- Synergistic effect

Example:

- β -lactam + aminoglycoside $\rightarrow$ enhanced bacterial killing

Disadvantages:

- Increased toxicity
- Drug interactions
- Superinfection

Resistance in Chemotherapy

- **Microorganisms may develop resistance by:**

- Enzyme production (e.g., β -lactamases)
- Target modification
- Reduced drug entry
- Increased drug efflux

Resistance Mechanisms

1. **Drug Efflux Pumps:** P-glycoprotein pumps drug out of cells
2. **Drug Inactivation:** Increased detoxifying enzymes
3. **Target Modification:** Mutation in drug target
4. **DNA Repair Enhancement:** Cancer cells repair drug-induced damage
5. Decreased Drug Uptake

Spectrum of Activity

1. Narrow Spectrum

- Effective against specific organisms
- **Example:** Penicillin G (mainly Gram-positive)

2. Broad Spectrum

- Effective against many organisms
- **Example:** Tetracyclines

Clinical importance:

- Broad-spectrum $\rightarrow$ useful in unknown infections

- But can cause **superinfection** (e.g., Candida overgrowth)

Toxicity (General)

- Bone marrow suppression (dose-limiting)
- Nausea and vomiting
- Hair loss (alopecia)
- Organ toxicity (heart, kidney, liver depending on drug)

Factors Affecting Drug Choice

- Site of infection (e.g., brain, lungs)
- Type of organism
- Patient factors (age, immunity, renal function)
- Drug toxicity profile
- Resistance patterns

β-Lactam Antibiotics (Mechanism & Resistance)

Basic Structure

- Contain a β-lactam ring → essential for activity

Classes

- Penicillins
- Cephalosporins
- Carbapenems
- Monobactams

Mechanism of Action (Cellular & Molecular)

Target: Bacterial Cell Wall

- Cell wall made of peptidoglycan
- Provides strength and protection

Step-by-Step Mechanism:

- β-lactam binds to Penicillin-Binding Proteins (PBPs)
- These are enzymes (transpeptidases)
- Inhibits cross-linking of peptidoglycan chains
- Weak cell walls are formed

- Bacterial cells undergoes osmotic lysis
- → **Result: Bactericidal effect**

Important Features

- Only active against actively dividing bacteria
- More effective on Gram-positive bacteria (thick cell wall)

Resistance Mechanisms

1. β -Lactamase Enzyme Production

- Bacteria produce enzymes that break the β -lactam ring
- Drug becomes inactive
- **Examples:**
 - Penicillinase
 - Extended-spectrum β -lactamases (ESBLs)

2. Alteration of PBPs

- PBPs change → drug cannot bind
- **Example:**
 - MRSA (Methicillin-resistant Staphylococcus aureus)

3. Reduced Drug Permeability

- Especially in Gram-negative bacteria
- Drug cannot enter through porin channels

4. Efflux Pumps

- Drug is actively pumped out of bacterial cell

Clinical Implications

- Combine with β -lactamase inhibitors (e.g., clavulanic acid)
- Resistance is a major clinical problem
- Requires careful antibiotic selection

Aminoglycosides (Mechanism & Resistance)

Examples

- Gentamicin
- Amikacin

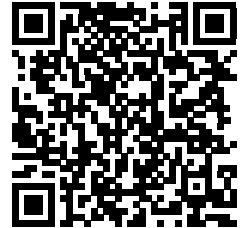


FREE PREVIEW

[Click here to visit our website](#)

PHARMACY PREMIUM NOTES

Complete subject
and semesters are
available on
FirstHope app only.



[Scan or click here](#)

Click here to get the app



Available on Google Play

JOIN THE FIRSTHOPE COMMUNITY

Join our Telegram channel

Click here to join Telegram



[Scan or click here](#)

@FirstHopeNotes

Instagram

@firsthope.official

[Click here to follow >](#)

YouTube channel

FirstHope-Pharmacy / Live streams

[Click here to watch >](#)

WhatsApp channel

Follow FirstHope on WhatsApp

[Click here to join >](#)

FirstHope website

firsthopenotes.com

[Click here to visit >](#)

B.Pharm / D.Pharm / M.Pharm / Pharm.D

Preview notes. Complete subjects and semesters in the FirstHope app.