BP506T · B.PHARM THEORY

Systemic Pharmacology II

Unit III — Chemotherapy

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

B.Pharm Semester V · Unit III · 14 Hours

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Chapter 1 — Introduction to Chemotherapy

1.1 Learning Objectives

By the end of this chapter, you will be able to:

1. Define chemotherapy, chemotherapeutic index, antibiotics, and antimicrobial agents.
2. Explain the concept of selective targeting (selective toxicity) in chemotherapy.
3. Classify antimicrobial agents based on their mechanism of action.
4. Explain superinfection, chemoprophylaxis, and the combined use of antibiotics.
5. Describe the causes, mechanisms, and preventive measures of antimicrobial resistance.
6. Discuss the pharmacist's role in the rational use of antimicrobials (antibiotic stewardship).

1.2 Definitions

Chemotherapy. Chemotherapy means the treatment of a disease with chemical substances (drugs) that are able to kill or stop the growth of the disease-causing agent without damaging the patient's body too much. The word comes from Greek: chemo = chemical, therapy = treatment.

- **Simple meaning:** using medicines (chemicals) to kill germs or cancer cells.
- **Example:** taking amoxicillin to kill the bacteria causing a throat infection; giving anticancer drugs to kill cancer cells.
- **Important:** chemotherapy does not mean only cancer treatment. In this unit, "chemotherapy" mainly means treatment of **infections** (antimicrobial chemotherapy) and also treatment of **cancer** (antineoplastic chemotherapy).

Antibiotic. An antibiotic is a substance produced by a microorganism (or made synthetically like it) that, in low concentrations, kills or stops the growth of other microorganisms. Originally, antibiotics came only from natural sources (e.g., penicillin from the Penicillium mould). Today many are semi-synthetic or fully synthetic, but the name "antibiotic" is used for all antibacterial drugs.

- **Simple meaning:** a medicine that kills bacteria or stops them from growing.
- **Example:** penicillin, amoxicillin, ciprofloxacin.

Antimicrobial agent. An antimicrobial agent is a broader term: any drug (natural, semi-synthetic, or synthetic) that kills or stops the growth of any microbe — bacteria, fungi, viruses, or parasites. So all antibiotics are antimicrobials, but not all antimicrobials are antibiotics (e.g., antifungal drugs and antiviral drugs are antimicrobials but are not called antibiotics).

- **Simple meaning:** any medicine that acts against germs (bacteria, fungi, viruses, parasites).

Chemotherapeutic index (CI). The chemotherapeutic index is a measure of the safety of a chemotherapeutic drug. It is the ratio between the dose that kills the parasite/microbe and the dose that harms the host (patient).

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Chemotherapeutic index = Toxic dose to the host / Effective dose against the microbe
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- **Simple meaning:** how safe the drug is — a high index means the drug kills the germ long before it harms the patient.
- **Example:** A drug that cures infection at 10 mg but harms the patient only at 500 mg has CI = 500/10 = 50 (good, safe). A drug with CI close to 1 is dangerous — the effective and toxic doses are nearly the same.

1.3 Terminology Table

Term	Simple meaning
Chemotherapy	Treatment of disease with drugs that kill the disease-causing agent
Chemotherapeutic index	Safety margin of a chemotherapeutic drug (toxic dose ÷ effective dose)
Antibiotic	Drug that kills or stops bacteria (originally from microorganisms)
Antimicrobial agent	Any drug acting against microbes (bacteria, fungi, viruses, parasites)
Selective toxicity	Killing the germ without harming the patient
Bactericidal	Kills bacteria (e.g., penicillin)
Bacteriostatic	Stops bacterial growth; body immunity then clears them (e.g., tetracycline)
Spectrum of activity	Range of microbes a drug acts against (narrow vs broad spectrum)
MIC (Minimum Inhibitory Concentration)	Lowest drug concentration that stops visible growth of the microbe
Superinfection	New infection by a different microbe during treatment of the first
Chemoprophylaxis	Giving drugs to prevent infection before it occurs
Antimicrobial resistance (AMR)	Microbes no longer killed by a drug that once worked
Antibiotic stewardship	Organized programme to ensure right antibiotic, right dose, right duration

1.4 Concept of Selective Targeting (Selective Toxicity)

Technical concept: Selective toxicity means a drug harms the infecting microorganism but not the human host. This is the whole basis of chemotherapy.

Simple explanation: Chemotherapy works because germs are different from human cells. The drug attacks something the germ has but human cells don't have (or have in a very different form). Like a key that fits the lock on the germ's door but doesn't fit any door in the human body.

Examples of selective targets:

Microbe has...	Human cells have...	Drug exploits this
Cell wall (peptidoglycan)	No cell wall	Penicillins destroy cell wall — harmless to humans
70S ribosomes	80S ribosomes (different shape)	Aminoglycosides block 70S — less effect on human 80S
Folic acid made by the bacterium itself	Humans get folic acid from food (no need to make it)	Sulphonamides block bacterial folic acid synthesis
Ergosterol in cell membrane	Cholesterol in cell membrane	Amphotericin B attacks ergosterol
Thymidine kinase enzyme (virus-infected cells)	Not used by normal cells the same way	Acyclovir gets activated only in virus-infected cells

Key takeaway: The bigger the difference between the germ and the human cell, the safer the drug. This is why penicillin (attacks bacterial cell wall, which humans lack) is so safe, while anticancer drugs (attack dividing cells — and human cells also divide) are much more toxic.

1.5 Classification of Antimicrobial Agents Based on Mechanism of Action

This is the master classification you must learn. Every drug in this unit fits into one of these five groups.

Master Table — Classification by Mechanism of Action

S.No.	Mechanism	What the drug does	Drug classes / examples
1	**Inhibit cell wall synthesis**	Stop the bacterium building its wall → cell bursts	Penicillins, cephalosporins, carbapenems, monobactams
2	**Damage cell membrane**	Punch holes in the cell membrane → contents leak out	Amphotericin B, nystatin, polymyxins
3	**Inhibit protein synthesis**	Block the bacterial ribosome → no new proteins	Macrolides, tetracyclines, chloramphenicol, aminoglycosides, linezolid
4	**Inhibit nucleic acid synthesis**	Stop DNA/RNA copying → germ cannot multiply	Fluoroquinolones (DNA gyrase), rifampicin (RNA polymerase), metronidazole
5	**Antimetabolites (block metabolic pathways)**	Block folic acid / essential chemical steps	Sulphonamides, trimethoprim (cotrimoxazole)

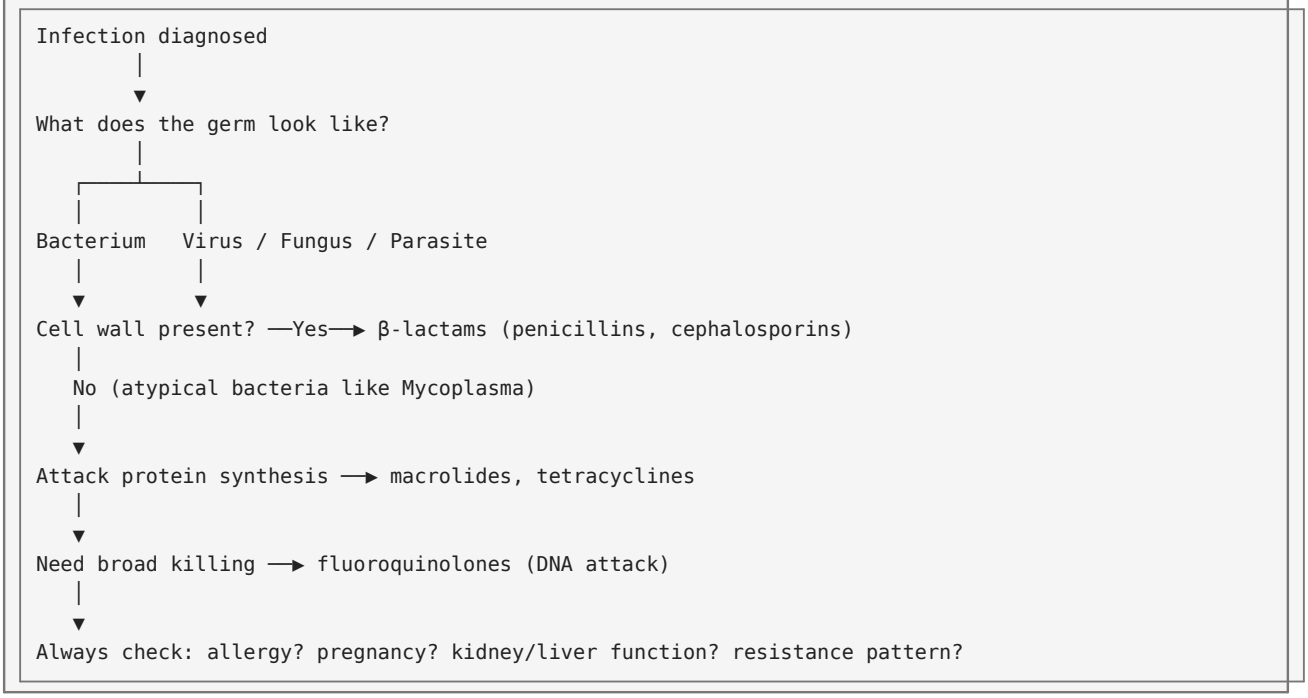
Diagram (to draw): "Five Doors" — mechanisms of antimicrobial action

Draw a bacterial cell as a large circle. Label five attack points with arrows:

1. Arrow to the **outer wall** — label: "Wall builders blocked (penicillins, cephalosporins)" — the wall cracks.
2. Arrow to the **membrane** — label: "Membrane punctured (amphotericin B)" — holes drawn in membrane.
3. Arrow to a small **ribosome** inside — label: "Protein factory stopped (tetracycline, macrolides)".
4. Arrow to a coiled **DNA** inside — label: "DNA copying blocked (fluoroquinolones)".
5. Arrow to a small **factory** labelled "folic acid plant" — label: "Raw material supply cut (sulphonamides)".

Caption: "Antimicrobials attack five targets. Human cells lack most of these targets — that is selective toxicity."

Flowchart: Choosing a drug by mechanism



Infographic Concept Box — "The 5 Mechanisms"

> 🎯 **5 ways to defeat a germ** > 🧱 **Break the wall** — penicillins, cephalosporins > 🕳️ **Puncture the membrane** — amphotericin B > 🏭 **Shut the protein factory** — macrolides, tetracyclines, aminoglycosides > 🧬 **Jam the photocopier (DNA)** — fluoroquinolones > 🚫 **Cut the raw material (folic acid)** — sulphonamides + trimethoprim > **Exam tip:** If you remember these 5 mechanisms, you can place ANY antimicrobial drug in the right box.

1.6 Superinfection

Definition: Superinfection is a new infection caused by a different microorganism that appears during (or shortly after) treatment of the original infection with an antimicrobial drug.

Simple explanation: Antibiotics kill not only the bad bacteria but also the good, friendly bacteria living in our gut, mouth, and skin. These friendly bacteria normally guard the area and keep harmful microbes out. When the guards are killed by a broad-spectrum antibiotic, a new enemy (often a resistant bacterium or a fungus) moves in and causes a second infection. That second infection is the superinfection.

Example: A patient takes a broad-spectrum antibiotic for pneumonia. The antibiotic kills gut bacteria too. The fungus Candida (normally kept in check by gut bacteria) now grows freely → the patient gets oral thrush (white patches in the mouth) or antibiotic-associated diarrhoea. This is superinfection.

Analogy: Spraying pesticide on a farm kills the pests but also the friendly insects that eat weed seeds. With the friendly insects gone, weeds take over the field. The weeds are the superinfection.

Common superinfecting organisms: Candida albicans (fungus), Clostridioides difficile (causes severe diarrhoea — pseudomembranous colitis), resistant Staphylococcus or Pseudomonas.

Prevention: use narrow-spectrum antibiotics when possible; avoid unnecessarily long courses; consider probiotics as advised by the physician.

1.7 Chemoprophylaxis

Definition: Chemoprophylaxis is the use of antimicrobial drugs to **prevent** an infection in a person who is at risk but not yet infected (or to prevent recurrence).

Simple explanation: Instead of waiting for the disease to attack, the medicine is given in advance as a shield.

Examples:

- A traveller going to a malaria-prone area takes antimalarial tablets before and during the trip → prevents malaria.
- A patient undergoing heart valve surgery receives antibiotics before surgery → prevents surgical site infection.
- A child with rheumatic fever takes monthly penicillin injections for years → prevents recurrence of rheumatic fever.
- People exposed to a meningitis patient receive preventive antibiotics.

Difference from treatment: Treatment = drug given after infection to cure it. Prophylaxis = drug given before infection to prevent it. Prophylaxis usually uses shorter courses and sometimes lower doses.

1.8 Combined Use of Antibiotics (Combination Therapy)

Definition: Using two or more antimicrobial drugs together to treat an infection.

Rationale — why combine? (simple reasons)

1. **To cover unknown germs (empirical therapy):** When the patient is seriously ill and the exact germ is not yet known, a combination covers many possibilities. Example: a combination for severe pneumonia covers both typical and atypical bacteria.
2. **To get a stronger, synergistic effect:** Sometimes 1 + 1 = 3. Example: penicillin + aminoglycoside for enterococcal endocarditis — penicillin damages the bacterial wall, letting the aminoglycoside enter easily. The combined killing is greater than the sum.
3. **To prevent resistance:** In TB and leprosy, using one drug alone quickly breeds resistant germs; combining 2–3 drugs makes it nearly impossible for the germ to become resistant to all at once (multidrug therapy).
4. **To treat mixed infections:** Some infections involve more than one germ (e.g., abdominal infections with both aerobic and anaerobic bacteria).

Rules of combination — when NOT to combine:

- Do not combine two **bacteriostatic** drugs that compete, or a bacteriostatic drug with a bactericidal one that needs growing bacteria (e.g., tetracycline + penicillin can antagonize, because penicillin kills only growing bacteria while tetracycline stops growth). Simple: don't mix "freezer" and "killer" drugs carelessly.
- Do not combine drugs with the **same toxicity** (e.g., two kidney-damaging drugs together) unless the benefit clearly outweighs the risk.
- Do not combine just to "be safe" — unnecessary combinations increase cost, side effects, and resistance.

Key takeaway: Combine with a purpose (synergy, coverage, resistance prevention); never combine blindly.

1.9 Antimicrobial Resistance (AMR)

Definition: Antimicrobial resistance is the ability of microorganisms to survive and grow despite the presence of an antimicrobial drug that previously killed them or stopped their growth.

Simple explanation: The drug used to work; now the germ has learned to dodge it. The medicine becomes useless against that germ.

(a) Causes of resistance

1. **Overuse and misuse of antibiotics** — taking antibiotics for viral cold/flu (where they cannot work), self-medication, stopping the course early ("I feel better, so I stopped").
2. **Incomplete courses** — stopping early leaves the strongest germs alive; they multiply and pass on their toughness.
3. **Overuse in animals and agriculture** — antibiotics used as growth promoters in poultry/livestock breed resistant germs that reach humans through food.
4. **Poor infection control in hospitals** — resistant germs spread between patients (e.g., MRSA in wards).
5. **Natural mutation** — germs multiply fast and mutate; some mutations accidentally give protection.
6. **Lack of new antibiotics** — few new drugs are being developed, so we depend on old ones.

(b) Mechanisms of resistance — how germs fight back

Mechanism	Simple explanation	Example
1. **Drug-destroying enzymes**	The germ makes an enzyme that cuts up the drug before it can act	**Beta-lactamase** enzyme destroys penicillins; extended-spectrum beta-lactamases (ESBL) destroy many cephalosporins
2. **Altered target**	The germ changes the shape of the lock so the drug-key no longer fits	MRSA changes its penicillin-binding protein (PBP2a) → methicillin/penicillins fail; altered ribosome → macrolide resistance
3. **Efflux pumps**	The germ installs "pumps" in its wall that throw the drug out as fast as it enters	Tetracycline resistance — pumps push tetracycline out of the cell
4. **Decreased permeability**	The germ closes its entry doors (porins) so the drug cannot get in	Loss of porin channels → resistance to some beta-lactams
5. **Alternative pathway**	The germ builds a bypass road around the blocked step	Bacteria use preformed folic acid from surroundings → sulphonamide resistance

Diagram (to draw): "Five shields of the resistant bacterium" Draw a bacterium with five labelled shields: (1) scissors cutting a drug molecule — "enzyme destroys drug (beta-lactamase)"; (2) a changed lock — "target changed"; (3) a pump throwing drug molecules out — "efflux pump"; (4) closed doors — "entry blocked"; (5) a bypass arrow around a roadblock — "alternative pathway".

(c) Preventive measures — including antibiotic stewardship

1. **Use antibiotics only when needed** — confirm bacterial infection; never for common cold/viral flu.
2. **Complete the full course** as prescribed.
3. **Correct dose and duration** — underdosing breeds resistance.
4. **Culture and sensitivity testing** — choose the drug the lab proves will work, especially in serious infections.
5. **Combination therapy** where indicated (TB, leprosy, H. pylori) to prevent resistance.
6. **Infection control** — hand hygiene, isolation of infected patients in hospitals.
7. **Antibiotic stewardship programmes** — hospital teams (doctors + pharmacists + microbiologists) that set antibiotic policies, restrict reserve antibiotics, audit prescriptions, and educate prescribers.
8. **Control antibiotic use in animals/agriculture**; avoid self-medication and over-the-counter sale of antibiotics.

Pharmacy relevance: The pharmacist is the gatekeeper. Do not dispense antibiotics without a valid prescription; counsel every patient to complete the course; report suspected treatment failures; participate in hospital stewardship committees.

1.10 India Context

- India carries one of the world's highest burdens of antimicrobial resistance. Over-the-counter sale of antibiotics without prescription and self-medication are major drivers.
- Hospital-acquired resistant infections (e.g., MRSA, ESBL-producing and carbapenem-resistant Gram-negative bacteria) are a serious concern in Indian tertiary hospitals.

- The Government of India runs the **National Programme on AMR Containment**; Schedule H1 of the Drugs Rules restricts over-the-counter sale of certain higher-generation antibiotics.
- As a future pharmacist, you will be on the front line: every prescription you screen and every patient you counsel on completing the antibiotic course directly fights AMR.

1.11 Key Points

1. Chemotherapy = treatment of disease (infections and cancer) with drugs that selectively harm the disease agent.

2. Chemotherapeutic index = toxic dose ÷ effective dose; higher = safer.

3. Antibiotics act against bacteria; antimicrobials act against all microbes (bacteria, fungi, viruses, parasites).

4. Selective toxicity is the foundation: drugs attack targets present in microbes but absent/different in humans.

5. Five mechanisms: (1) cell wall inhibition, (2) membrane damage, (3) protein synthesis inhibition, (4) nucleic acid inhibition, (5) antimetabolites.

6. Superinfection = new infection by a different microbe during antibiotic treatment (normal flora destroyed).

7. Chemoprophylaxis = drugs given to prevent infection.

8. Combine antibiotics for synergy, broad coverage, or resistance prevention — never blindly.

9. Resistance mechanisms: drug-destroying enzymes, altered targets, efflux pumps, reduced entry, bypass pathways.

10. Prevent AMR by rational use, full courses, culture-guided therapy, infection control, and stewardship.

1.12 Common Confusions

Confusion	Clarification
"Chemotherapy means only cancer treatment"	No — chemotherapy means drug treatment of any disease agent; antimicrobial chemotherapy and cancer chemotherapy are both chemotherapy.
Antibiotic vs antimicrobial	Antimicrobial is the bigger umbrella; antibiotic (strictly) = antibacterial.
Bactericidal is always better than bacteriostatic	Not always — in some infections (e.g., meningitis, endocarditis) bactericidal is preferred, but bacteriostatic drugs cure many infections with the help of immunity.
"Stronger antibiotic" means better	Wrong — the right (narrow, sensitive) antibiotic is better than a broad "strong" one; broad use breeds resistance and superinfection.
Resistance means the patient's body became resistant	No — the germ becomes resistant, not the patient.

1.13 Common Mistakes

1. Writing that penicillin kills viruses — it does not; antibiotics do not act on the common cold or flu.

2. Defining chemotherapeutic index upside-down (effective ÷ toxic). It is toxic ÷ effective.

3. Listing "cell wall synthesis inhibition" for drugs like tetracycline (it inhibits protein synthesis).

4. Forgetting that superinfection is caused by a different organism, not relapse of the same one.

5. In exams, giving vague resistance mechanisms — name the five with one example each.

1.14 Mnemonics

- **Five mechanisms — "We Make People Never Miss":** **W**all (β-lactams), **M**embrane (amphotericin), **P**rotein synthesis (macrolides etc.), **N**ucleic acid (fluoroquinolones), **M**etabolite block (sulphonamides).
- **Resistance mechanisms — "DEEAB":** **D**estroy drug (enzymes), **E**fflux pumps, **E**ntry blocked, **A**ltered target, **B**ypass pathway.
- **Bactericidal vs static:** "**Cidal** kills (like homi**cidal**); **static** stays (like **static** electricity — nothing moves)."

1.15 Exam Summary

Chemotherapy is drug treatment that selectively destroys disease-causing agents (microbes, cancer cells) while sparing the host — this selectivity is called selective toxicity, and its margin is measured by the chemotherapeutic index (toxic dose/effective dose). Antimicrobials are classified by mechanism into five groups: cell-wall inhibitors, membrane damagers, protein-synthesis inhibitors, nucleic-acid inhibitors, and antimetabolites. Superinfection is a second infection by a new organism during antibiotic therapy due to destruction of normal flora; chemoprophylaxis is preventive drug use; antibiotic combinations are used for synergy, empirical coverage, or resistance prevention but must follow rules (avoid antagonistic pairs and overlapping toxicities). Antimicrobial resistance arises from misuse, incomplete courses, and mutations, operating through drug-destroying enzymes (beta-lactamase), altered targets, efflux pumps, reduced permeability, and bypass pathways; it is prevented by rational use, culture-guided therapy, full courses, infection control, and antibiotic stewardship.

1.16 One-Minute Revision

- Chemo = chemical treatment of disease agents; CI = toxic/effective.
- Selective toxicity: attack what the germ has and humans don't.
- 5 mechanisms: wall, membrane, protein, DNA, folate.
- Superinfection: new germ during treatment (flora killed). Prophylaxis: prevent before. Combos: synergy/coverage/resistance — with rules.
- Resistance: enzymes, altered target, efflux, blocked entry, bypass. Prevent: rational use + stewardship.

1.17 Exam Questions

Short answers (2–3 marks)

1. Define chemotherapy and chemotherapeutic index. Give the formula for chemotherapeutic index.

2. Differentiate between an antibiotic and an antimicrobial agent with one example each.

3. What is selective toxicity? Give two examples of selective targets.
4. Define superinfection and give one example with the causative organism.
5. What is chemoprophylaxis? Give two examples.
6. Name the five mechanisms of antimicrobial resistance with one example each.

Long answers (10 marks)

1. Classify antimicrobial agents based on their mechanism of action, giving two drug examples for each class.
2. Discuss the causes, mechanisms, and preventive measures of antimicrobial resistance. Add a note on antibiotic stewardship.
3. Explain the concept of selective targeting in chemotherapy with suitable examples. Why are penicillins considered safe drugs?
4. What is the combined use of antibiotics? Discuss its rationale, rules, and disadvantages with examples.

MCQs (answer key at end)

1. The chemotherapeutic index is:

a) Effective dose / toxic dose b) Toxic dose / effective dose c) Dose / body weight d) MIC / MBC

1. Which of the following is a selective target present in bacteria but absent in human cells?

a) 80S ribosome b) Cell wall peptidoglycan c) Cholesterol d) Nucleus

1. Sulphonamides act by:

a) Inhibiting cell wall synthesis b) Blocking folic acid synthesis c) Damaging cell membrane d) Inhibiting DNA gyrase

1. Superinfection is most commonly caused by:

a) The same organism relapsing b) A different organism, e.g., Candida, after normal flora destruction c) Viral mutation d) Allergic reaction

1. Beta-lactamase causes resistance by:

a) Pumping the drug out b) Destroying the beta-lactam drug enzymatically c) Changing the ribosome d) Closing porin channels

1. Which combination shows synergy?

a) Tetracycline + penicillin b) Penicillin + aminoglycoside in endocarditis c) Two nephrotoxic drugs together d) Bacteriostatic + bactericidal without reason

1. Chemoprophylaxis means:

a) Treatment after infection b) Drug use to prevent infection c) Combined drug therapy d) Treatment of superinfection

1. MRSA is resistant to methicillin due to:

a) Beta-lactamase production b) Altered penicillin-binding protein (PBP2a) c) Efflux pumps d) Bypass pathway

Answer key: 1-b, 2-b, 3-b, 4-b, 5-b, 6-b, 7-b, 8-b.

Viva questions (with answers)

1. **Q: What is the difference between bactericidal and bacteriostatic?**

A: Bactericidal drugs kill bacteria (e.g., penicillin); bacteriostatic drugs only stop their growth, and the body's immunity clears them (e.g., tetracycline).

1. **Q: Why don't antibiotics work against the common cold?**

A: The common cold is caused by viruses; antibiotics act on bacterial targets (cell wall, bacterial ribosomes) which viruses lack.

1. **Q: Name one drug from each of the five mechanism classes.**

A: Wall — amoxicillin; membrane — amphotericin B; protein synthesis — azithromycin; nucleic acid — ciprofloxacin; antimetabolite — cotrimoxazole.

1. **Q: What is antibiotic stewardship?**

A: An organized hospital programme ensuring the right antibiotic, right dose, and right duration, to improve outcomes and slow resistance.

1. **Q: Give one example each of superinfection and chemoprophylaxis.**

A: Superinfection — oral thrush by Candida during broad-spectrum antibiotic therapy. Prophylaxis — antimalarial tablets before travel to an endemic area.

Application-based questions

1. A patient stops his 7-day antibiotic course on day 3 because he feels better. Two weeks later the infection returns and the same antibiotic no longer works. Explain what happened using the concepts of this chapter.

2. A surgeon asks you (the pharmacist) why a single antibiotic injection before surgery is preferred over a 5-day postoperative antibiotic course for a clean surgery. Justify using chemoprophylaxis principles.

3. A hospital wants to start an antibiotic stewardship programme. As a pharmacist, list five concrete actions you would propose.

1.18 References

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Chapter 2 — Antimicrobial Agents

2.1 Learning Objectives

By the end of this chapter, you will be able to:

1. Classify each antimicrobial class in the syllabus and recall key drug examples.
2. Explain the mechanism of action of each class in simple terms.
3. Describe the spectrum of activity of each class.
4. List the major adverse drug reactions of each class.
5. State the therapeutic uses of each class.
6. Use simple mnemonics to recall drug names and their key toxicities.

2.2 Definitions

Beta-lactam antibiotics. Antibiotics containing a beta-lactam ring in their structure — penicillins, cephalosporins, carbapenems, and monobactams. They all inhibit bacterial cell-wall synthesis.

Beta-lactamase. A bacterial enzyme that breaks the beta-lactam ring and destroys the antibiotic — the commonest cause of penicillin resistance.

Generations (of cephalosporins/fluoroquinolones). Successive groups of newer drugs in the same family; each generation usually has a broader spectrum or better properties than the previous one.

Aminoglycosides. A group of antibiotics (gentamicin, amikacin, streptomycin, etc.) that kill bacteria by blocking protein synthesis; famous for kidney and ear toxicity.

2.3 Terminology Table

Term	Simple meaning
Beta-lactam ring	The common chemical ring in penicillins/cephalosporins that does the killing work
Beta-lactamase inhibitor	A drug (e.g., clavulanic acid) that blocks the bacterial enzyme, protecting the antibiotic
PBP (penicillin-binding protein)	The bacterial wall-building enzyme that beta-lactams switch off
Generation	Newer, improved version-group within a drug family
Ototoxicity	Damage to the ear (hearing loss, balance problems)
Nephrotoxicity	Damage to the kidneys
Photosensitivity	Skin becoming extra-sensitive to sunlight
Grey baby syndrome	Serious toxicity of chloramphenicol in newborns (ashen-grey colour, collapse)
Red man syndrome	Flushing/itching reaction with fast vancomycin infusion (not in syllabus detail, mentioned for awareness)
Cross-allergy	Allergy to one drug causing allergy to a related drug (penicillin ↔ cephalosporin)

2.4 Sulphonamides and Cotrimoxazole

Classification

Sulphonamides are classified by duration of action:

- **Short-acting:** sulphadiazine

- **Intermediate-acting:** sulphamethoxazole (the "sulpha" in cotrimoxazole)
- **Long-acting:** sulphadoxine (used with pyrimethamine in malaria — see Chapter 3)
- **Topical/local:** silver sulphadiazine (burns), sulfacetamide eye drops

Cotrimoxazole = fixed combination of **trimethoprim + sulphamethoxazole** (usually in a 1:5 ratio). It is the most important drug of this group today.

Mechanism of action

Technical: Sulphonamides block the bacterial enzyme dihydropteroate synthase, stopping folic acid synthesis. Trimethoprim blocks the next step, dihydrofolate reductase. Together they produce sequential blockade of folic acid synthesis — a double block.

Simple explanation: Bacteria need to cook their own folic acid (a vitamin they need to grow) in a two-step kitchen process. Sulphonamide locks the first cooking station; trimethoprim locks the second. With both stations locked, the bacterium starves and cannot multiply. Human cells are safe because we get folic acid ready-made from food — we don't run this kitchen at all.

Diagram (to draw): "Double lock on the folic acid kitchen" Draw two boxes in sequence: Box 1 "PABA → (enzyme 1)" with a padlock labelled "sulphonamide locks here"; Box 2 "→ folic acid (enzyme 2)" with a padlock labelled "trimethoprim locks here". Below, draw a human figure eating food with a tick mark: "Humans get folate from food — kitchen not needed." Title: "Sequential blockade — why cotrimoxazole is stronger than either drug alone."

Key takeaway: Cotrimoxazole = double blockade of folic acid synthesis = bactericidal synergy.

Spectrum

Broad — many Gram-positive and Gram-negative bacteria; also Pneumocystis jirovecii, Toxoplasma, Nocardia.

Adverse drug reactions

- Nausea, vomiting, loss of appetite
- **Skin rashes**; rarely severe reactions (Stevens–Johnson syndrome)
- **Blood disorders:** fall in white cells/platelets, haemolytic anaemia (especially in G6PD deficiency)
- **Kernicterus risk in newborns:** sulphonamides displace bilirubin from blood proteins — avoid in newborns and late pregnancy
- Crystalluria (crystals in urine) — prevented by drinking plenty of water
- Trimethoprim can raise blood potassium

Therapeutic uses

- **Urinary tract infections** (uncomplicated)
- **Pneumocystis pneumonia** (in immunocompromised patients) — treatment and prophylaxis
- Toxoplasmosis, nocardiosis
- Traveller's diarrhoea, shigellosis (where sensitive)
- Silver sulphadiazine cream for burn wounds

Memory hook

"Co-TRIM locks the second door" — cotrimoxazole = sulphamethoxazole (first step) + TRIMethoprim (second step). **"Sulpha harms the newborn's brain (kernicterus)"** — remember the newborn warning.

2.5 Fluoroquinolones

Classification (by generation)

- **First generation:** nalidixic acid (urinary only, not a true fluoroquinolone by some texts)
- **Second generation: ciprofloxacin**, ofloxacin, norfloxacin
- **Third generation:** levofloxacin (the active "left-handed" form of ofloxacin)
- **Fourth generation:** moxifloxacin, gemifloxacin (better Gram-positive and anaerobic cover)

Memory hook: "**C**ipro for **C**lassic second-gen" — ciprofloxacin is the prototype you must know.

Mechanism of action

Technical: Fluoroquinolones inhibit bacterial **DNA gyrase** (topoisomerase II) and **topoisomerase IV** — enzymes that unwind and reseal DNA during copying. Blocking them causes fatal breaks in bacterial DNA.

Simple explanation: When a bacterium wants to divide, it must photocopy its DNA instruction book. Two helper enzymes untwist and rejoin the pages during copying. Fluoroquinolones handcuff these helpers — the pages tear, and the bacterium dies. Human cells have different versions of these enzymes, so they are mostly spared (selective toxicity again).

Analogy: Like jamming a photocopier mid-copy — the machine tears the paper and stops forever.

Spectrum

Very broad — Gram-negative bacteria (including Pseudomonas for ciprofloxacin), many Gram-positive, atypical organisms; newer generations cover anaerobes too. Excellent for urinary, gut, and respiratory infections.

Adverse drug reactions

- Nausea, diarrhoea, headache, dizziness
- **Tendon damage / tendon rupture** (especially Achilles tendon, in elderly and with steroids) — the famous "quinolone tendon" warning
- **CNS effects:** insomnia, confusion, rarely seizures
- **Photosensitivity** (skin burns easily in sunlight)
- **Cartilage damage in children** — generally avoided in children and pregnancy
- QT prolongation (heart rhythm) with some agents; Clostridioides difficile diarrhoea risk
- **Drug interaction:** antacids/iron/zinc bind quinolones in the gut and block absorption — separate by 2–3 hours

Therapeutic uses

- **Urinary tract infections** (ciprofloxacin, norfloxacin)
- Typhoid fever, bacterial diarrhoea, traveller's diarrhoea
- Respiratory infections (levofloxacin, moxifloxacin — "respiratory quinolones")
- Bone/joint infections, prostatitis, anthrax exposure prophylaxis (ciprofloxacin)

Memory hook

"FLOX the DNA photocopier" — all names end in **-floxacin**. **"Torn Tendons"** — tendon rupture is the signature toxicity.

2.6 Penicillins and Cephalosporins

Classification of penicillins

1. **Natural penicillins:** penicillin G (injection), penicillin V (oral) — narrow, mainly Gram-positive
2. **Penicillinase-resistant penicillins:** cloxacillin, dicloxacillin — kill staph that make penicillinase
3. **Aminopenicillins (extended spectrum): amoxicillin**, ampicillin — wider, some Gram-negative
4. **Antipseudomonal penicillins:** piperacillin (with tazobactam) — covers Pseudomonas
5. **Beta-lactamase inhibitor combinations:** amoxicillin + clavulanic acid (co-amoxiclav), piperacillin + tazobactam

Classification of cephalosporins (by generation)

Generation	Key drugs	Spectrum trend	Typical use
1st	**cefazolin** (inj.), cephalexin (oral)	Strong Gram-positive	Surgical prophylaxis, skin infections
2nd	cefuroxime, cefoxitin	More Gram-negative, some anaerobes	Respiratory, mixed infections
3rd	**ceftriaxone**, cefotaxime, ceftazidime	Broad Gram-negative; ceftazidime covers Pseudomonas	Meningitis, sepsis, gonorrhoea (ceftriaxone)
4th	cefepime	Broad, resists many beta-lactamases	Serious hospital infections
5th	ceftaroline	Covers MRSA	Resistant Gram-positive infections

Memory hook: "**Cef** = cephalosporin; generations go **Z-U-T-E**: cefa**Z**olin (1st), cef**U**roxime (2nd), cef**T**riaxone (3rd), cefa**E**pime (4th)."

Mechanism of action

Technical: Beta-lactams bind **penicillin-binding proteins (PBPs)** — the enzymes that cross-link peptidoglycan in the bacterial cell wall — and switch them off. Without cross-linking, the wall weakens and the bacterium bursts (osmotic lysis). They act only on **growing** bacteria.

Simple explanation: Bacteria wear a hard "armour" (cell wall) that humans don't have. Beta-lactams switch off the workers building this armour. As the bacterium tries to grow, its half-built armour cracks and the cell bursts like an overfilled balloon. Because humans have no such armour, these drugs are among the safest antibiotics.

Diagram (to draw): "The bursting balloon" Draw two bacteria side by side. Left: normal bacterium with a thick brick wall labelled "peptidoglycan wall — intact". Right: bacterium with cracked, crumbling wall and contents spilling out, labelled "beta-lactam switched off wall builders → wall cracks → cell bursts". Add a human cell nearby with a speech bubble: "No wall here — I'm safe."

Key takeaway: Beta-lactams = wall-breakers = bactericidal, very safe, but useless against bacteria with no wall (Mycoplasma) or with beta-lactamase.

Spectrum

Penicillins: streptococci, meningococci, syphilis (Treponema), clostridia; aminopenicillins add E. coli, Haemophilus; piperacillin adds Pseudomonas. Cephalosporins: progressively broader Gram-negative cover with each generation.

Adverse drug reactions

- **Allergy is the big one:** rashes to **anaphylaxis** (life-threatening) — always ask about penicillin allergy before giving
- **Cross-allergy:** a penicillin-allergic patient may also react to cephalosporins
- Diarrhoea (especially amoxicillin-clavulanate), nausea
- Ceftriaxone: gallbladder sludge/pseudostones; must not be mixed with calcium-containing IV fluids in newborns
- Rare: blood disorders, seizures with very high doses

Therapeutic uses

- Streptococcal sore throat, rheumatic fever prophylaxis (penicillin)
- Syphilis (penicillin G — still the drug of choice)
- Pneumonia, meningitis (ceftriaxone/cefotaxime)
- Surgical prophylaxis (cefazolin)
- Skin/soft-tissue infections, urinary infections (cephalexin, cefuroxime)
- Severe hospital infections (piperacillin-tazobactam, cefepime)

Memory hook

"Always Ask Allergy" — the first question before any penicillin/cephalosporin. **"Ceftriaxone — one shot for gonorrhoea, meningitis cover."**

2.7 Macrolides and Tetracyclines

Classification

- **Macrolides: erythromycin**, **azithromycin**, clarithromycin, roxithromycin
- **Tetracyclines: tetracycline**, **doxycycline**, minocycline, tigecycline

Memory hook: Macrolides end in **-thromycin**; tetracyclines end in **-cycline**.

Mechanism of action

Technical: Both bind the bacterial **50S (macrolides) or 30S (tetracyclines) ribosomal subunit** and block protein synthesis — macrolides block the growing protein chain from leaving; tetracyclines block the entry of new amino-acid carriers.

Simple explanation: The bacterial ribosome is a protein factory with two floors — 50S (upper) and 30S (lower). Macrolides jam the exit door on the upper floor; tetracyclines block the raw-material entry on the lower floor. Either way, no proteins get made and the bacterium cannot grow or repair itself. Human factories (80S ribosomes) have a different shape, so they are mostly unaffected.

Diagram (to draw): "Two floors of the protein factory" Draw a factory with two floors labelled 50S (top) and 30S (bottom). On the top floor, a macrolide molecule blocks a door labelled "protein exit — jammed by -thromycins". On the bottom floor, a tetracycline molecule blocks a conveyor belt labelled "raw material entry — blocked by -cyclines". Caption: "Same factory, two different sabotage points."

Spectrum

- **Macrolides:** Gram-positive cocci, **atypical organisms** (Mycoplasma, Chlamydia, Legionella), some Gram-negative; the choice in penicillin-allergic patients

- **Tetracyclines:** Very broad — rickettsia, chlamydia, mycoplasma, cholera (Vibrio), acne bacteria, anthrax, Lyme disease

Adverse drug reactions

- **Macrolides:** nausea, abdominal cramps, diarrhoea (erythromycin stimulates gut movement); QT prolongation (azithromycin — heart rhythm caution); liver irritation; drug interactions (erythromycin/clarithromycin block liver enzymes → raise levels of many drugs)
- **Tetracyclines:** nausea, diarrhoea, **photosensitivity**; **teeth discolouration and bone growth problems in children under 8 and in pregnancy — never give to them**; liver toxicity in high doses; **chelation** — calcium, iron, antacids bind tetracycline in the gut and stop absorption (take on empty stomach, separate from milk/antacids)

Therapeutic uses

- **Macrolides:** respiratory infections, atypical pneumonia (Mycoplasma), whooping cough, chlamydia (azithromycin single dose), alternative in penicillin allergy
- **Tetracyclines: acne** (doxycycline), cholera, rickettsial fevers, chlamydia, Lyme disease, malaria prophylaxis (doxycycline — see Chapter 3)

Memory hook

"No -cyclines for kids under eight — yellow teeth!" (teeth staining). **"Azithro for Atypical"** — azithromycin covers atypical pneumonia organisms.

2.8 Linezolid

Classification

Oxazolidinone — the first of a newer class; reserved antibiotic.

Mechanism of action
Technical: Binds the **50S ribosomal subunit** at an early step, preventing formation of the initiation complex — protein synthesis never even starts. **Simple explanation:** While macrolides jam the factory's exit door, linezolid stops the workers from even entering the factory in the morning. No start, no proteins.

Spectrum

Narrow but precious: **Gram-positive** bacteria including resistant ones — **MRSA** and **vancomycin-resistant enterococci (VRE)**.

Adverse drug reactions

- **Bone marrow suppression** (low platelets, anaemia) with use beyond ~2 weeks — blood counts must be monitored
- **Optic nerve and peripheral nerve damage** with prolonged use
- Lactic acidosis (rare); nausea, diarrhoea, headache
- **Serotonin syndrome** risk if combined with certain antidepressants (SSRIs)

Therapeutic uses

- **Reserve drug** for MRSA pneumonia, skin infections, and VRE infections when standard drugs fail

- Used only when needed — overuse would breed linezolid resistance and waste a precious reserve

Memory hook

"Linezolid is the Last Line for resistant Gram-positives" — MRSA and VRE. **"Lines cross the marrow"** — watch blood counts.

2.9 Carbapenems and Monobactams

Classification

- **Carbapenems: imipenem** (+ cilastatin), **meropenem**, ertapenem, doripenem
- **Monobactam: aztreonam** (only one in common use)

Memory hook: Carbapenems end in **-penem**; the monobactam is **aZTreonam** (think "**A**lone — the **one** monobactam").

Mechanism of action

Technical: Like penicillins, they bind PBPs and inhibit cell-wall synthesis. Carbapenems resist destruction by most beta-lactamases (including ESBLs); aztreonam binds mainly the PBP of Gram-negative bacteria.

Simple explanation: Carbapenems are the "special forces" beta-lactams — same wall-breaking attack as penicillin, but wearing armour against the bacterial beta-lactamase scissors. Aztreonam is a sniper that only shoots Gram-negative bacteria.

Spectrum

- **Carbapenems:** broadest of all beta-lactams — Gram-positive, Gram-negative (including ESBL producers), anaerobes; meropenem covers Pseudomonas
- **Aztreonam: only Gram-negative aerobes** including Pseudomonas; no Gram-positive or anaerobic cover

Adverse drug reactions

- Nausea, diarrhoea, rashes
- **Imipenem can cause seizures** (especially in kidney failure or brain disorders) — meropenem is safer in this regard
- Imipenem is broken down by a kidney enzyme, so it is always given with **cilastatin**, which blocks that enzyme
- Aztreonam: generally well tolerated; **safe in penicillin-allergic patients** (almost no cross-allergy) — its special advantage

Therapeutic uses

- **Carbapenems:** reserve drugs for serious hospital infections resistant to other antibiotics (ESBL infections, complicated intra-abdominal infections, hospital-acquired pneumonia)
- **Aztreonam:** Gram-negative infections in **penicillin-allergic** patients

Memory hook

"PeneMs are the ultiMate weapons — keep them in reserve." "Aztreonam = Allergic patients' friend."

2.10 Chloramphenicol and Aminoglycosides

Chloramphenicol

Classification: A broad-spectrum antibiotic, one of the oldest; now a reserve drug because of its toxicity.

Mechanism: Binds the **50S ribosomal subunit** and blocks protein synthesis (like macrolides, different binding spot).

Simple explanation: Another factory saboteur on the 50S floor — but this one is dangerous to the human "head office" (bone marrow), so it is kept locked away for emergencies only.

Spectrum: Very broad — Gram-positive, Gram-negative, anaerobes, rickettsia; still used for bacterial **meningitis** and **typhoid** where needed, and as eye drops/ointment for eye infections.

Adverse drug reactions — the ones examiners love:

- **Grey baby syndrome** in newborns: the newborn liver cannot detoxify chloramphenicol → ashen-grey colour, vomiting, collapse, can be fatal — **never give to newborns**
- **Aplastic anaemia:** rare but fatal bone-marrow failure (unpredictable, not dose-related) — the reason for its restricted use

Therapeutic uses: Bacterial meningitis, typhoid (reserve), eye infections (topical).

Memory hook: "**Grey** baby, **grave** marrow — chloramphenicol's two killers."

Aminoglycosides

Classification: gentamicin, **amikacin**, **streptomycin**, tobramycin, neomycin (topical/oral only).

Memory hook: Most end in **-micin** (genta**micin**, ami**kacin**).

Mechanism: Bind the **30S ribosomal subunit**, causing misreading of the genetic code — the bacterium makes **faulty, garbage proteins** and dies. Bactericidal. They need oxygen to enter bacteria, so they **do not work on anaerobes**.

Simple explanation: Aminoglycosides don't just stop the factory — they corrupt the instruction manual, so the bacterium builds broken machines from wrong parts and dies. But they can only enter bacteria that "breathe" oxygen.

Spectrum: Mainly **Gram-negative aerobes** (E. coli, Klebsiella, Pseudomonas); streptomycin is a first-line **anti-TB** drug (see Chapter 3); combined with penicillin for endocarditis (synergy).

Adverse drug reactions — the famous pair:

- **Ototoxicity:** damage to the ear — hearing loss and balance disturbance (can be permanent)
- **Nephrotoxicity:** kidney damage (usually reversible if caught early)
- Neuromuscular blockade in high doses (muscle weakness)

Therapeutic uses: Serious Gram-negative hospital infections (with a beta-lactam), TB (streptomycin), endocarditis (gentamicin + penicillin synergy), topical (neomycin).

Memory hook: "**Amino-glycosides attack the Ear and the Kidney — oto + nephro**, remember the pair." "**Garbage proteins** — they corrupt the code."

Master comparison table — all antimicrobial classes of this unit

Class	Prototype drugs	Mechanism	Bactericidal / static	Signature toxicity
Sulphonamides + cotrimoxazole	Sulphamethoxazole + trimethoprim	Block folic acid synthesis (double block)	Static (cidal as combo)	Rash, blood disorders, kernicterus (newborn)
Fluoroquinolones	Ciprofloxacin, levofloxacin	Block DNA gyrase/topoisomerase	Cidal	Tendon rupture, CNS effects, photosensitivity
Penicillins	Amoxicillin, cloxacillin	Block cell-wall synthesis (PBPs)	Cidal	**Allergy/anaphylaxis**
Cephalosporins	Cefazolin, ceftriaxone	Block cell-wall synthesis (PBPs)	Cidal	Allergy (cross with penicillin)
Macrolides	Azithromycin, erythromycin	Block 50S protein synthesis	Static	GI upset, QT prolongation
Tetracyclines	Doxycycline	Block 30S protein synthesis	Static	**Teeth staining in children**, photosensitivity
Linezolid	Linezolid	Block 50S initiation	Static/cidal	Bone marrow suppression
Carbapenems	Meropenem, imipenem	Block cell-wall synthesis (beta-lactamase-proof)	Cidal	Seizures (imipenem)
Monobactam	Aztreonam	Block cell-wall synthesis (Gram-negative only)	Cidal	Few; safe in penicillin allergy
Chloramphenicol	Chloramphenicol	Block 50S protein synthesis	Static	**Grey baby syndrome, aplastic anaemia**
Aminoglycosides	Gentamicin, amikacin	Corrupt 30S protein synthesis	Cidal	**Ototoxicity + nephrotoxicity**

Flowchart: which class for which situation?

```
Serious bacterial infection
        |
        ▼
Penicillin allergy? ──Yes──▶ macrolide / aztreonam (Gram-negative) / fluoroquinolone
        | No
        ▼
Need cell-wall killer? ──Yes──▶ penicillin / cephalosporin (check generation needed)
        |
        ▼
Resistant hospital bug (ESBL)? ──Yes──▶ carbapenem (meropenem) — reserve
        |
        ▼
MRSA / VRE? ──Yes──▶ linezolid — reserve
        |
        ▼
Atypical organism (Mycoplasma)? ──Yes──▶ macrolide / doxycycline
        |
        ▼
Need Gram-negative killing fast? ──▶ aminoglycoside + beta-lactam (synergy, watch ear + kidney)
```

Infographic Concept Box — "Know your killer by its ending"

> 🧠 **Drug-name endings that tell you the family** > **-cillin** → penicillin (amoxi**cillin**) > **cef-/ceph-** → cephalosporin (**cef**triaxone) > **-penem** → carbapenem (mero**penem**) > **-floxacin** → fluoroquinolone (cipro**floxacin**) > **-thromycin** → macrolide (azi**thromycin**) > **-cycline** → tetracycline (doxy**cycline**) > **-micin/-mycin** → aminoglycoside (genta**micin**) — careful: erythro**mycin** is a macrolide! > **Exam tip:** endings are the fastest way to classify an unknown drug name in MCQs.

2.11 Pharmacy Relevance

- **Allergy history:** before dispensing any penicillin/cephalosporin, confirm the patient has no penicillin allergy — anaphylaxis kills within minutes.
- **Counselling points:** take fluoroquinolones/tetracyclines away from antacids, iron, and milk; drink extra water with sulphonamides; avoid sunlight with photosensitizing drugs; complete the full course.
- **Reserve drugs:** linezolid, carbapenems — dispense only on valid prescription; never substitute casually; support hospital antibiotic policy.
- **Paediatric/pregnancy vigilance:** no tetracyclines under 8 years or in pregnancy; no chloramphenicol in newborns; caution with fluoroquinolones in children.
- **Monitoring:** aminoglycosides — watch kidney function and hearing; linezolid beyond 2 weeks — blood counts.

2.12 India Context

- **Cotrimoxazole** remains widely used in India for UTIs and is part of prophylaxis regimens for immunocompromised patients.
- **Ciprofloxacin** was once the mainstay for typhoid in India; rising resistance has shifted therapy (see Chapter 3 notes on typhoid).
- **Ceftriaxone** is among the most-used injectable antibiotics in Indian hospitals — and also among the most misused; stewardship programmes target it specifically.
- **Amikacin and meropenem** are critical reserve drugs in Indian ICUs against carbapenem-resistant organisms; their overuse directly drives resistance.
- **Streptomycin** retains a defined role in India's TB programme (see Chapter 3).

2.13 Key Points

1. Cotrimoxazole = sulphamethoxazole + trimethoprim = double blockade of folic acid synthesis.

2. Fluoroquinolones jam DNA gyrase/topoisomerase; signature toxicity = tendon rupture; avoid in children/pregnancy.

3. All beta-lactams (penicillins, cephalosporins, carbapenems, monobactam) block cell-wall synthesis via PBPs; the signature danger is allergy/anaphylaxis.

4. Cephalosporin generations: 1st (cefazolin) → 5th (ceftaroline, covers MRSA); broader Gram-negative cover with each generation.

5. Macrolides (50S) and tetracyclines (30S) block protein synthesis; macrolides cover atypical organisms; tetracyclines stain children's teeth — never under 8 years.

6. Linezolid = reserve oxazolidinone for MRSA/VRE; watch bone marrow.

7. Carbapenems = broadest beta-lactams, beta-lactamase-proof, reserve use; imipenem needs cilastatin and can cause seizures.

8. Aztreonam = only Gram-negative; safe in penicillin allergy.

9. Chloramphenicol = grey baby syndrome + aplastic anaemia = restricted use.

10. Aminoglycosides corrupt 30S protein synthesis; signature toxicities = ototoxicity + nephrotoxicity; inactive against anaerobes.

2.14 Common Confusions

Confusion	Clarification
Erythromycin ends in -mycin, so it must be an aminoglycoside	No — erythromycin is a **macrolide**; the -mycin ending is shared. Learn the drug, not just the ending.
All beta-lactams are destroyed by beta-lactamase	No — carbapenems and penicillinase-resistant penicillins (cloxacillin) resist it; that's their special value.
Aztreonam covers all bacteria	No — Gram-negative aerobes only.
Bacteriostatic drugs are useless	They cure many infections with immune help; e.g., doxycycline cures cholera and chlamydia.
Linezolid can be used as first-line for any infection	No — it is a reserve drug for resistant Gram-positive infections (MRSA, VRE).

2.15 Common Mistakes

1. Writing "fluoroquinolones inhibit cell-wall synthesis" — they inhibit DNA enzymes.

2. Forgetting that aminoglycosides need oxygen — writing them for anaerobic infections.

3. Prescribing tetracycline to a 5-year-old in a case question — teeth staining; choose a macrolide instead.

4. Mixing up which subunit: macrolides = 50S, tetracyclines = 30S, aminoglycosides = 30S (but corrupt, not just block).

5. Forgetting cilastatin with imipenem, or the seizure risk of imipenem.

2.16 Mnemonics

- **Beta-lactam allergy:** "**P**enicillin **P**roblem = **P**atient may **P**erish (anaphylaxis)" — always ask.
- **Aminoglycoside toxicities:** "**A**mino **E**ar **K**idney" — **oto**toxicity + **nephro**toxicity.
- **Tetracycline in kids:** "**T**eeth **T**urn **T**awny (yellow-brown) — no **T**etracycline till eight."
- **Chloramphenicol:** "**C**hloro = **C**ollapse (grey baby) + **C**ancelled marrow (aplastic anaemia)."
- **Quinolone tendon:** "**Flox** and your **Achilles** may **part** (rupture)."
- **Sulpha + trimeth:** "**S**ulpha **S**tops **S**tep one, **T**rimeth **T**raps **T**ep two."

2.17 Exam Summary

Sulphonamides and trimethoprim (cotrimoxazole) sequentially block bacterial folic acid synthesis. Fluoroquinolones inhibit DNA gyrase and topoisomerase IV, killing bacteria by shattering DNA; their hallmark toxicity is tendon rupture. Penicillins, cephalosporins (five generations, broadening Gram-negative cover), carbapenems (beta-lactamase-resistant, reserve), and the monobactam aztreonam (Gram-negative only, safe in penicillin allergy) all inhibit cell-wall synthesis via penicillin-binding proteins; allergy/anaphylaxis is their chief danger. Macrolides (50S), tetracyclines (30S), chloramphenicol (50S), and linezolid (50S initiation) inhibit protein synthesis — macrolides cover atypical organisms, tetracyclines are barred in children under eight and pregnancy (teeth/bone), chloramphenicol is restricted (grey baby syndrome, aplastic anaemia), and linezolid is reserved for MRSA/VRE (marrow suppression). Aminoglycosides corrupt 30S protein synthesis, killing Gram-negative aerobes, with ototoxicity and nephrotoxicity as signature toxicities.

2.18 One-Minute Revision

- Cotrimoxazole: double folate block. Sulpha: rash, kernicterus in newborns.
- Floxacins: DNA gyrase; tendon rupture; not in kids.
- Beta-lactams: wall-breakers; allergy kills — always ask.
- Cephalosporin generations 1→5: cefazolin → cefuroxime → ceftriaxone → cefepime → ceftaroline (MRSA).
- Macrolide 50S (atypical cover); tetracycline 30S (no kids <8, no milk/antacid together).
- Linezolid: MRSA/VRE reserve; watch blood counts.
- Carbapenems: broadest, reserve; imipenem + cilastatin, seizure risk.
- Aztreonam: Gram-negative only; penicillin-allergy safe.
- Chloramphenicol: grey baby + aplastic anaemia.
- Aminoglycosides: garbage proteins; ear + kidney toxicity.

2.19 Exam Questions

Short answers

1. Explain the mechanism of action of cotrimoxazole with a labelled diagram.
2. Classify cephalosporins by generation with one example each.
3. Why are fluoroquinolones avoided in children and pregnancy?
4. Explain the synergy between penicillin and aminoglycoside with one clinical example.
5. List the signature toxicities of chloramphenicol and aminoglycosides.
6. Why is cilastatin combined with imipenem?
7. What is the special advantage of aztreonam in penicillin-allergic patients?

Long answers

1. Classify penicillins. Describe their mechanism of action, adverse effects, and therapeutic uses.
2. Discuss fluoroquinolones: classification by generation, mechanism of action, spectrum, adverse effects, and uses.
3. Compare macrolides, tetracyclines, chloramphenicol, and aminoglycosides with respect to ribosomal target, spectrum, key toxicities, and uses.

4. Write notes on: (a) carbapenems, (b) linezolid — covering classification, mechanism, spectrum, adverse effects, and why they are reserve drugs.

MCQs

1. Cotrimoxazole blocks:

a) Cell-wall synthesis b) Folic acid synthesis at two steps c) DNA gyrase d) 50S ribosome

1. Tendon rupture is classically associated with:

a) Penicillins b) Fluoroquinolones c) Macrolides d) Tetracyclines

1. Which cephalosporin generation does ceftriaxone belong to?

a) First b) Second c) Third d) Fifth

1. Grey baby syndrome is caused by:

a) Tetracycline b) Chloramphenicol c) Gentamicin d) Sulphadiazine

1. Aminoglycosides are ineffective against anaerobes because:

a) Anaerobes lack ribosomes b) Their uptake into bacteria requires oxygen c) Anaerobes make beta-lactamase d) They are destroyed by acid

1. Teeth discolouration in children is caused by:

a) Amoxicillin b) Tetracycline c) Azithromycin d) Ciprofloxacin

1. The drug safe in penicillin-allergic patients with Gram-negative infection:

a) Amoxicillin b) Aztreonam c) Cefazolin d) Piperacillin

1. Linezolid is reserved for:

a) Viral infections b) MRSA and VRE infections c) Fungal infections d) Malaria

1. Imipenem is combined with cilastatin to:

a) Increase absorption b) Prevent its breakdown by kidney enzymes c) Reduce allergy d) Add synergy

1. Which statement about macrolides is TRUE?

a) They bind the 30S subunit b) They cover atypical organisms like Mycoplasma c) They are first-line for Pseudomonas d) They stain teeth in children

Answer key: 1-b, 2-b, 3-c, 4-b, 5-b, 6-b, 7-b, 8-b, 9-b, 10-b.

Viva questions (with answers)

1. **Q: Why is cotrimoxazole more powerful than sulphamethoxazole alone?**

A: Sequential double blockade of folic acid synthesis — sulphamethoxazole blocks the first enzyme, trimethoprim the second; the combination is synergistic and bactericidal.

1. **Q: A child with pneumonia is allergic to penicillin. Which class would you suggest and why?**

A: A macrolide (e.g., azithromycin) — covers common and atypical pneumonia organisms and is safe in penicillin allergy.

1. **Q: Why must antacids be separated from ciprofloxacin doses?**

A: Calcium/magnesium/iron in antacids bind (chelate) the quinolone in the gut, preventing absorption.

1. **Q: Name two reserve antibiotics and the infections they are reserved for.**

A: Meropenem — resistant Gram-negative hospital infections; linezolid — MRSA/VRE.

1. **Q: What monitoring is needed for a patient on gentamicin?**

A: Kidney function (serum creatinine) and hearing/balance symptoms — nephrotoxicity and ototoxicity.

Application-based questions

1. A 6-year-old with chlamydial eye infection is prescribed tetracycline eye ointment by mistake (systemic course). Identify the error, explain the risk, and suggest the correct alternative class.

2. An elderly patient on ciprofloxacin for a UTI, also taking prednisolone, complains of sudden Achilles heel pain. What is the likely cause? What would you advise as the pharmacist?

3. A hospital's ICU reports rising ESBL Klebsiella infections. The committee proposes restricting ceftriaxone and reserving meropenem. Justify this stewardship decision using resistance concepts from Chapter 1.

2.20 References

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Chapter 3 — Chemotherapy of Diseases

3.1 Learning Objectives

By the end of this chapter, you will be able to:

1. Name the causative agents of nine disease groups: fungal, viral, helminthic, urinary tract, TB, leprosy, malaria, amoebiasis, and neoplastic diseases.
2. List the drug classes and key drugs used for each disease and explain why each drug is chosen (link to mechanism).
3. Describe the major adverse effects of these drugs.
4. Explain resistance concepts: MDR-TB, antimalarial resistance, and why multidrug therapy is used in TB/leprosy.
5. Describe India's national programmes and burden for TB, leprosy, and malaria.
6. Counsel patients on completing long treatments (TB, leprosy) and on prophylaxis (malaria).

3.2 Definitions

MDR-TB (multidrug-resistant tuberculosis). TB caused by Mycobacterium tuberculosis resistant to at least the two most powerful first-line drugs, isoniazid and rifampicin.

DOTS / NTEP. India's National TB Elimination Programme (earlier called RNTCP/DOTS) — provides free diagnosis and directly observed treatment for TB.

Chemoprophylaxis (malaria). Taking antimalarial drugs before/during travel to endemic areas to prevent infection.

Anthelmintic. A drug that kills or expels parasitic worms (helminths).

Antineoplastic. A drug used against cancer (neoplasm = new abnormal growth).

3.3 Terminology Table

Term	Simple meaning
Mycobacterium tuberculosis	The bacterium causing TB; has a waxy wall, grows very slowly
M. leprae	The bacterium causing leprosy; cannot be grown in the lab
Plasmodium	The parasite causing malaria (species: vivax, falciparum, malariae, ovale)
Entamoeba histolytica	The parasite causing amoebiasis (amoebic dysentery, liver abscess)
Helminth	Parasitic worm (roundworm, tapeworm, hookworm, filarial worm)
UTI	Urinary tract infection — infection of bladder (cystitis) or kidney (pyelonephritis)
MDR-TB / XDR-TB	TB resistant to 2+ first-line drugs (MDR); plus resistance to second-line drugs (XDR)
NTEP	National TB Elimination Programme of India
NLEP	National Leprosy Eradication Programme of India
Antimetabolite (cancer)	Anticancer drug that mimics normal cell building blocks and jams DNA synthesis

3.4 Fungal Infections — Chemotherapy

Causative agents (in brief)

Fungi causing human disease: Candida albicans (thrush, vaginal candidiasis, systemic), Aspergillus (lung/systemic in immunocompromised), dermatophytes (ringworm, athlete's foot), Cryptococcus (meningitis in immunocompromised), Mucor (mucormycosis).

Drug classes and key drugs — and why chosen

Class	Key drugs	Why chosen (mechanism link)
Polyenes	**Amphotericin B**, nystatin	Bind **ergosterol** in fungal cell membrane → punch holes → cell contents leak. Selective: human membranes have cholesterol, not ergosterol.
Azoles	**Fluconazole**, itraconazole, ketoconazole, clotrimazole (topical), voriconazole	Block the fungal enzyme making **ergosterol** → membrane weakens. Broad, many are oral.
Echinocandins	Caspofungin, micafungin	Block fungal **cell-wall** (glucan) synthesis — human cells have no wall, so very selective.
Allylamines	Terbinafine	Block an early step of ergosterol synthesis; concentrates in skin/nails — ideal for ringworm.
Antimetabolite	Flucytosine	Converted inside fungal cells to a false building block that jams fungal DNA/RNA.

Simple story: Fungi build their houses with a special brick called ergosterol; human houses use cholesterol. Antifungals either smash the ergosterol bricks (amphotericin B), stop the brick factory (azoles, terbinafine), or break the fungal wall (echinocandins).

Major adverse effects

- **Amphotericin B: fever, chills during infusion; kidney damage; low potassium/magnesium** — the most toxic antifungal; given as slow IV infusion with monitoring (lipid formulations are safer but costly)
- **Azoles:** nausea, liver irritation (monitor liver function); many drug interactions (they block liver enzymes); ketoconazole — hormone-related effects
- **Terbinafine:** generally safe; taste disturbance, liver caution
- **Flucytosine:** bone marrow suppression

Resistance notes

Azole resistance occurs in some Candida species (efflux pumps — the same pump concept from Chapter 1); combination therapy (amphotericin B + flucytosine) is used for cryptococcal meningitis to prevent resistance.

Memory hook: "**Ampho-terrible** for the kidney — B stands for 'Bad kidneys'." "**Azoles** end in **-azole** and block the ergosterol factory."

3.5 Viral Infections — Chemotherapy

Causative agents (in brief)

Viruses are not cells — they hijack human cells to multiply. Examples: HIV, herpes simplex (cold sores), varicella-zoster (chickenpox/shingles), hepatitis B and C, influenza, SARS-CoV-2.

Key concept: Antivirals are harder to design than antibiotics because viruses use the human cell's own machinery — fewer selective targets (recall Chapter 1: selective toxicity needs differences).

Drug classes and key drugs — and why chosen

Infection	Key drugs	Why chosen (mechanism link)
Herpes (HSV, VZV)	**Acyclovir**, valacyclovir	Activated **only in virus-infected cells** by viral thymidine kinase → then jams viral DNA copying. Beautiful selective toxicity: uninfected cells barely activate it.
HIV	**NRTIs** (zidovudine, tenofovir), **NNRTIs** (efavirenz), **protease inhibitors** (ritonavir-boosted), **integrase inhibitors** (dolutegravir)	Block three viral steps: reverse transcriptase (copying RNA→DNA), protease (cutting viral proteins), integrase (inserting viral DNA). Used as **combinations (ART)** — never single drug, to prevent resistance.
Hepatitis B	Tenofovir, entecavir	Block viral DNA polymerase.
Hepatitis C	Direct-acting antivirals (sofosbuvir-based combos)	Block viral enzymes; cure rates very high.
Influenza	Oseltamivir	Blocks neuraminidase — new virus particles cannot escape the cell.

Simple story: Antivirals are like saboteurs that only wake up inside enemy-occupied buildings (acyclovir), or that cut the enemy's three supply lines at once (HIV triple therapy).

Major adverse effects

- **Acyclovir:** generally safe; nausea, headache; kidney crystals if dehydrated — drink water
- **HIV drugs:** nausea, liver effects; zidovudine — anaemia; efavirenz — vivid dreams/CNS effects; long-term metabolic effects; **strict adherence is critical** — missed doses breed resistance fast
- **Oseltamivir:** nausea, vomiting

Resistance notes

HIV mutates rapidly — single-drug therapy fails quickly; **combination ART** (3 drugs) is mandatory. This is the same "don't let the germ escape through one door" logic as TB multidrug therapy.

Memory hook: "**A**cyclovir **A**ctivates in **A**ffected cells." "**HIV needs a TRIO** — triple therapy, always."

3.6 Helminthiasis — Chemotherapy

Causative agents (in brief)

Parasitic worms: roundworm (Ascaris), hookworm, threadworm/pinworm (Enterobius), tapeworm (Taenia), filarial worms (Wuchereria — elephantiasis), schistosomes (blood flukes).

Drug classes and key drugs — and why chosen

Drug	Main use	Why chosen (mechanism link)
Albendazole, mebendazole	Roundworm, hookworm, pinworm, tapeworm — broad worm killers	Block the worm's **microtubules** (its internal skeleton) → worm cannot absorb food → starves and dies. Selective: binds worm tubulin much more than human tubulin.
Praziquantel	Tapeworm, schistosomes (blood flukes)	Damages worm's skin, causes paralysis → worm detaches and is expelled.
Ivermectin	Filariasis, threadworm, scabies	Paralyzes the worm by opening chloride channels in its nerves.
Diethylcarbamazine (DEC)	Filariasis (elephantiasis)	Kills microfilariae (baby worms in blood); India's programme drug.
Piperazine	Roundworm/pinworm (older drug)	Paralyzes worms → expelled alive in stool.

Simple story: Deworming tablets either starve the worm (albendazole — breaks its food pipes), paralyze it (ivermectin, piperazine), or melt its skin (praziquantel) — then the body flushes it out.

Major adverse effects

Generally well tolerated: nausea, abdominal pain, headache. DEC in filariasis can cause allergic-type reactions as dying worms release proteins (fever, rash) — this is expected, not drug allergy.

Resistance notes

Less of a clinical problem in humans than in veterinary medicine, but mass deworming programmes monitor for reduced efficacy.

India context

India runs the **National Deworming Day** (schoolchildren receive albendazole); the **filariasis elimination programme** uses DEC + albendazole mass drug administration in endemic districts.

Memory hook: "**Al**bendazole kills **Al**l worms (broadest)." "**Praziquantel Prazi-es the flukes.**"

3.7 Urinary Tract Infections — Chemotherapy

Causative agents (in brief)

Mostly bacteria ascending from the gut: **Escherichia coli** (commonest by far), Klebsiella, Proteus, Enterococcus, Pseudomonas (hospital/complicated cases). Cystitis = bladder infection; pyelonephritis = kidney infection (more serious).

Drugs used — and why chosen

Drug/class	Why chosen
Nitrofurantoin	Concentrates in **urine**, not blood — perfect for bladder infection; little effect elsewhere. First choice for uncomplicated cystitis.
Cotrimoxazole	Good urine levels; broad cover (where resistance allows).
Ciprofloxacin / norfloxacin	Excellent urine and prostate penetration; used when first-line fails or in complicated UTI.
Fosfomycin (single dose)	Single-dose convenience for uncomplicated cystitis in women.
Cephalosporins (e.g., cefixime)	Alternative, also safe in pregnancy.
Amoxicillin	Used in pregnancy (safe option) where the organism is sensitive.

Simple story: For a bladder infection, pick a drug that lives in the urine (nitrofurantoin) — like sending the police to patrol exactly the street where the crime happens.

Major adverse effects

- Nitrofurantoin: nausea, brown urine (harmless), rare lung/liver effects with long use
- Fluoroquinolones: as in Chapter 2 (tendon, CNS, photosensitivity)
- General: diarrhoea, rashes

Resistance notes

E. coli resistance to cotrimoxazole and fluoroquinolones is rising in India — **urine culture and sensitivity** should guide therapy in recurrent/complicated UTI rather than repeated empirical courses.

Pharmacy relevance

Counsel: drink plenty of water, complete the course even if burning passes in 2 days, do not self-medicate with leftover antibiotics; pregnant patients need physician-chosen safe options.

Memory hook: "**Nitro-furantoin for the urine** — it goes where the infection is."

3.8 Tuberculosis — Chemotherapy

Causative agent (in brief)

Mycobacterium tuberculosis — a slow-growing bacterium with a thick **waxy wall** (mycolic acids) that makes it hard for drugs to enter and hard to stain; treatment must be long (months) because the germ grows slowly and hides inside cells.

Drugs used — first-line and second-line

First-line drugs (the famous four + streptomycin):

Drug	Why chosen (mechanism link)	Key adverse effects
Isoniazid (H)	Blocks **mycolic acid** (waxy wall) synthesis — the wall TB depends on	**Liver toxicity**; **peripheral neuritis** (tingling hands/feet — prevented with vitamin B6/pyridoxine);
Rifampicin (R)	Blocks bacterial **RNA polymerase** → no RNA → germ dies; kills dormant germs too	**Orange-red urine/tears/sweat** (harmless but warn the patient!); liver toxicity; **induces liver enzymes** → destroys contraceptive pills and many other drugs
Pyrazinamide (Z)	Kills germs hiding in **acidic** areas (inside cells)	Liver toxicity; **raised uric acid → gout-like joint pains**
Ethambutol (E)	Blocks wall (arabinogalactan) synthesis; mainly stops resistance	**Optic neuritis → blurred vision, colour blindness** — test vision regularly
Streptomycin (S)	Aminoglycoside — corrupts protein synthesis (injectable)	Ototoxicity + nephrotoxicity (Chapter 2)

Second-line / reserve drugs (for MDR-TB): fluoroquinolones (levofloxacin, moxifloxacin), bedaquiline, linezolid, clofazimine, cycloserine — used in longer, supervised regimens.

Why multidrug therapy? (links to Chapter 1)

TB germs mutate to resistance easily; a single drug would select resistant mutants within weeks. Using 3–4 drugs together means a germ would need simultaneous mutations against all — practically impossible. **Never treat TB with a single drug.**

Regimen concept (cautious wording)

Treatment has an **intensive phase** (more drugs, ~2 months) followed by a **continuation phase** (fewer drugs, ~4 months or longer). Exact regimens evolve — confirm from current National TB Elimination Programme guidelines.

MDR-TB concept

MDR-TB = TB resistant to at least isoniazid + rifampicin, the two strongest drugs. It arises mainly from **incomplete/irregular treatment** — the classic consequence of stopping medicines early. Treatment needs second-line drugs for much longer, with more side effects and lower cure rates. **XDR-TB** adds resistance to second-line drugs.

India context

- India has the world's **largest TB burden**; TB is a notifiable disease.
- The **National TB Elimination Programme (NTEP)** provides **free diagnosis and treatment**, including directly observed therapy and digital adherence support; the national goal is TB elimination.
- Pharmacists must **notify** TB cases and counsel every patient: take medicines daily for the full duration, never stop early, report vision changes (ethambutol), orange urine is harmless (rifampicin), and take pyridoxine if prescribed.

Memory hook — first-line five: "**H**eroes **R**arely **Z**ap **E**vil **S**wiftly" — **H** = isoniazid, **R** = rifampicin, **Z** = pyrazinamide, **E** = ethambutol, **S** = streptomycin. **Side-effect hook:** "**I**soniazid = **I**njures liver + nerves; **R**ifampicin = **R**ed urine; **P**yrazinamide = **P**ainful joints (uric acid); **E**thambutol = **E**yes."

Diagram (to draw): "Why TB needs 4 drugs"

Draw one TB bacterium surrounded by four drug "soldiers" labelled H, R, Z, E, each attacking a different part (wall, RNA, acidic hideout, wall-builder). Caption: "One drug = the germ learns one trick and escapes. Four drugs = no escape."

3.9 Leprosy — Chemotherapy

Causative agent (in brief)

Mycobacterium leprae — cousin of the TB bacterium; grows extremely slowly and **cannot be grown in laboratory culture**; affects skin and nerves.

Drugs used — multidrug therapy (MDT)

Drug	Why chosen (mechanism link)	Key adverse effects
Dapsone	Like sulphonamides — blocks **folic acid** synthesis in the leprosy bacillus	Blood disorders (haemolysis, especially G6PD deficiency), rash
Rifampicin	Kills leprosy bacilli fast (RNA polymerase block); monthly supervised dose	Orange urine/secretions; liver effects; enzyme induction
Clofazimine	Binds bacterial DNA; anti-inflammatory effect useful in reactions	**Reddish-brown skin discolouration** (reversible but distressing — warn the patient); dry skin

Why multidrug therapy?

Same logic as TB: dapsone alone bred resistant leprosy; **MDT (dapsone + rifampicin + clofazimine)** cures and prevents resistance. Duration depends on disease type (paucibacillary vs multibacillary) — confirm current NLEP guidance.

India context

- India achieved leprosy **elimination as a public health problem** (prevalence <1/10,000) but new cases still occur; the **National Leprosy Eradication Programme (NLEP)** provides free MDT.
- Stigma remains a bigger problem than the disease itself — cured patients need social support; pharmacists should counsel with sensitivity and confidentiality.

Memory hook: "**D**apsone **R**ifampicin **C**lofazimine — **D**efeat **R**esistance **C**ompletely." "**Clofazimine Colours the skin.**"

3.10 Malaria — Chemotherapy

Causative agents (in brief)

Plasmodium parasites transmitted by the bite of female Anopheles mosquitoes: **P. vivax** (commonest in India; forms dormant liver stages = relapses), **P. falciparum** (most dangerous — cerebral malaria), P. malariae, P. ovale.

Drugs used — and why chosen

Drug	Main use	Why chosen (mechanism link)	Key adverse effects
Chloroquine	P. vivax (sensitive areas)	Concentrates in parasite's food vacuole; blocks **haem detoxification** — the parasite digests haemoglobin and must detoxify the leftover haem; chloroquine jams this → parasite poisoned by its own waste	Generally safe; itching, nausea; eye damage only with years of use
Artemisinin-based combination therapies (ACTs) — artemether + lumefantrine etc.	**Uncomplicated P. falciparum** — first choice	Artemisinin creates **free radicals** inside the parasite → fastest parasite killing known; partner drug mops up survivors → combination prevents resistance	Nausea, dizziness; generally well tolerated
Primaquine	**Radical cure of P. vivax** (kills dormant liver stages → prevents relapse)	Kills liver hypnozoites	**Haemolysis in G6PD deficiency — test before giving**
Sulphadoxine + pyrimethamine	Falciparum (where still effective)	Double folate blockade (like cotrimoxazole logic)	Rash, blood effects
Quinine	Severe malaria (IV) where artesunate unavailable	Oldest antimalarial; blocks haem detoxification	**Cinchonism** (ringing in ears, headache, nausea), low blood sugar
Doxycycline	Prophylaxis / partner drug	Blocks parasite protein synthesis (30S-like)	Photosensitivity (Chapter 2)

Simple story: The malaria parasite eats the patient's haemoglobin and must bury the toxic leftover (haem). Chloroquine and quinine block the burial → the parasite drowns in its own garbage. Artemisinin is a bomb of free radicals that shreds the parasite in hours. Primaquine hunts the

sleeping forms in the liver.

Resistance notes

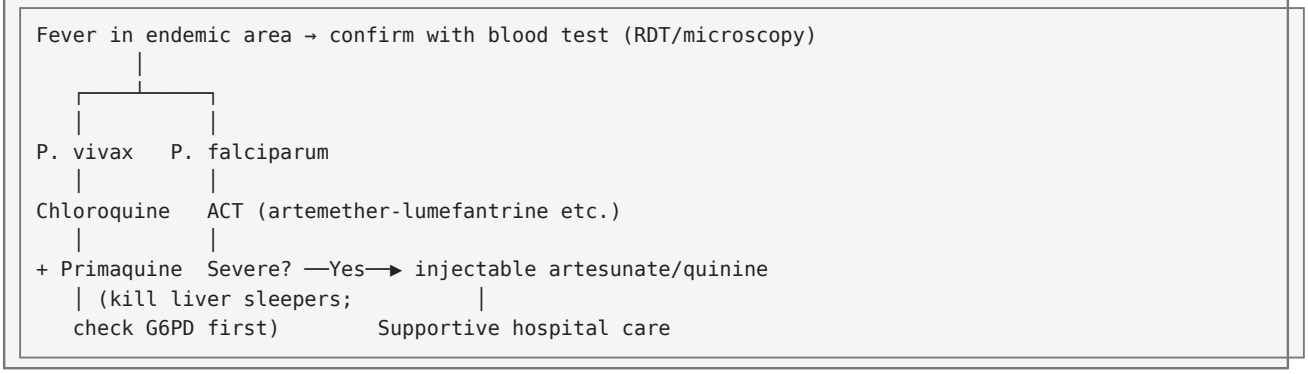
P. falciparum became resistant to chloroquine across much of India — hence ACTs are now first-line for falciparum. **Never use artemisinin alone** (monotherapy breeds resistance); always as a combination (ACT). This mirrors the TB/leprosy lesson.

India context

- Malaria is endemic in parts of **Odisha, Chhattisgarh, Jharkhand, Madhya Pradesh, and the Northeast**; P. vivax predominates nationally but falciparum dominates in high-burden pockets.
- India's national drug policy: ACT for falciparum, chloroquine + primaquine for vivax (regimens evolve — confirm current national guidelines).
- **Chemoprophylaxis** for travellers to endemic areas (e.g., doxycycline or atovaquone-proguanil as per current guidance).

Memory hook: "ACT fast for Falciparum; Primaquine Prevents vivax relapse." "Chloroquine Clogs the haem dustbin."

Flowchart: choosing malaria treatment (concept)



3.11 Amoebiasis — Chemotherapy

Causative agent (in brief)

Entamoeba histolytica — a gut parasite causing **amoebic dysentery** (bloody diarrhoea) and **liver abscess**; spreads through contaminated food/water.

Drugs used — and why chosen

Drug	Main use	Why chosen (mechanism link)	Key adverse effects
Metronidazole	**Tissue amoebiasis** — intestinal wall invasion and **liver abscess** (drug of choice)	In anaerobic organisms, it is converted to **toxic free radicals** that shred parasite DNA. Selective: only activated where oxygen is low (parasite's environment).	**Metallic taste**, nausea; **disulfiram-like reaction with alcohol — no alcohol during treatment**; headache, dark urine (harmless)
Diloxanide furoate	**Luminal (gut-cyst) amoebiasis** — kills cysts in the intestine	Kills the cyst forms metronidazole misses	Mild GI upset
Tinidazole	Alternative to metronidazole	Same family, longer acting	Similar to metronidazole

Treatment logic (must know): Metronidazole kills the invading tissue forms but not all gut cysts → follow with **diloxanide furoate** to clear the gut lumen and prevent relapse. **Simple:** metronidazole = soldier fighting inside the walls; diloxanide = guard sweeping the courtyard.

Memory hook: "**Metro** kills the **tissue**; **Diloxanide** does the **luminal** clean-up." "**No booze with Metro** (metronidazole) — alcohol reaction."

3.12 Neoplastic Diseases — Chemotherapy (Anticancer Drugs)

The problem (in brief)

Cancer = uncontrolled division of the body's own cells. **Selective toxicity is poor** here because cancer cells are human cells — drugs that kill dividing cancer cells also harm normal dividing cells (bone marrow, gut lining, hair roots). Hence anticancer drugs are the most toxic chemotherapeutic agents, with a **low chemotherapeutic index**.

Drug classes and key drugs — and why chosen

Class	Key drugs	Why chosen (mechanism link)	Key adverse effects
Alkylating agents	**Cyclophosphamide**, cisplatin	Attach alkyl groups to DNA → **cross-link DNA strands** → cell cannot copy DNA → dies	Bone marrow suppression, nausea/vomiting, hair loss; cyclophosphamide — bladder bleeding (haemorrhagic cystitis, prevented with fluids/MESNA); cisplatin — kidney damage, hearing loss
Antimetabolites	**Methotrexate**, 5-fluorouracil (5-FU)	**Fake building blocks** — look like normal DNA ingredients but jam the machinery (methotrexate blocks folic acid use in DNA synthesis)	Bone marrow suppression, mouth ulcers, diarrhoea; methotrexate — liver/lung effects
Plant alkaloids / mitotic inhibitors	**Vincristine**, vinblastine, paclitaxel	**Break the cell-division ropes** (microtubules) → cell cannot split in two	Vincristine — **nerve damage** (tingling, constipation); bone marrow suppression; hair loss
Antibiotics (anticancer)	Doxorubicin, bleomycin	Insert into DNA / break DNA strands	Doxorubicin — **heart damage** (cardiotoxicity, dose-limited); bone marrow suppression
Hormonal agents	Tamoxifen (breast cancer)	Blocks **oestrogen receptors** — starves hormone-dependent cancer	Hot flushes, clot risk
Targeted / immunotherapy (concept)	Monoclonal antibodies, checkpoint inhibitors	Attack specific cancer markers — better selectivity, newer approach	Varies; generally less marrow toxicity

Simple story: Anticancer drugs attack the cell-division machinery — photocopier (antimetabolites), the paper (alkylators cross-link it), the ropes pulling cells apart (vincristine). But every dividing healthy cell — hair, gut, marrow — gets caught in the crossfire. That's why hair falls, mouth ulcerates, and blood counts drop.

Major adverse effects (common to most)

Bone marrow suppression (infection/bleeding risk — the dose-limiting toxicity for most), **nausea/vomiting**, **hair loss (alopecia)**, mouth ulcers, diarrhoea. These occur because normal rapidly-dividing tissues are hit too — the price of poor selectivity.

Resistance notes

Cancer cells develop resistance by the same five tricks as bacteria (Chapter 1): drug pumps (efflux), altered targets, DNA repair, bypass pathways. Combination chemotherapy (multiple drugs, multiple mechanisms) is standard — same logic as TB/HIV.

India context

Cancer burden is rising in India (breast, cervical, oral, lung cancers lead). Government schemes support affordable cancer care; pharmacists in oncology handle safe preparation, extravasation management, antiemetic protocols, and counselling on what to expect (hair loss is temporary; report fever immediately — it may signal dangerously low white cells).

Memory hook: "**M**ethotrexate **M**imics folate; **C**yclophosphamide **C**ross-links; **V**incristine **V**andalizes microtubules; **D**oxorubicin **D**amages the heart."

Master table — Chapter 3 diseases at a glance

Disease	Key causative agent	First-choice drugs	Signature toxicity to remember
Fungal	Candida, Aspergillus	Amphotericin B, fluconazole	Ampho B — kidney damage
Viral (herpes)	HSV/VZV	Acyclovir	Safe; kidney crystals if dehydrated
Viral (HIV)	HIV	Triple ART (NRTI+NNRTI/PI/integrase inhibitor)	Adherence critical
Helminthiasis	Roundworm, filaria	Albendazole, DEC, ivermectin	Generally safe
UTI	E. coli	Nitrofurantoin, cotrimoxazole, ciprofloxacin	Rising resistance — culture-guided
TB	M. tuberculosis	H-R-Z-E (±S); MDR needs second-line	H: liver/nerves; R: red urine; Z: joints; E: eyes
Leprosy	M. leprae	Dapsone + rifampicin + clofazimine (MDT)	Clofazimine — skin colour change
Malaria	P. vivax / falciparum	Vivax: chloroquine + primaquine; falciparum: ACT	Primaquine — G6PD haemolysis
Amoebiasis	E. histolytica	Metronidazole + diloxanide furoate	No alcohol with metronidazole
Cancer	Own cells dividing wildly	Cyclophosphamide, methotrexate, vincristine, doxorubicin	Marrow suppression, hair loss, vomiting

Diagram (to draw): "Selectivity ladder"

Draw a ladder with four rungs. Bottom rung (widest, safest): "Penicillin — target absent in humans (cell wall)". Next: "Antifungals — target slightly different (ergosterol vs cholesterol)". Next: "Antivirals — few targets (virus hides in human cell)". Top rung (narrowest, most toxic): "Anticancer drugs — target shared with normal dividing cells". Caption: "The less different the target, the more toxic the drug — the whole story of chemotherapy in one ladder."

Infographic Concept Box — "One rule for TB, leprosy, HIV, malaria"

> □ **Never fight alone — the combination rule** > TB → 4 drugs (H-R-Z-E) · Leprosy → 3 drugs (MDT) · HIV → 3 drugs (ART) · Falciparum malaria → 2 drugs (ACT) > **Why?** One drug lets the germ learn one escape trick. Combinations attacking different targets make escape nearly impossible. > **Exam tip:** If a question asks "why multidrug therapy?", answer: to prevent resistance and achieve cure — then name the drugs.

3.13 Pharmacy Relevance

- **TB/leprosy counselling:** the single most important pharmacist job in this chapter — daily dosing for months, never stop early, report side effects (vision, orange urine is harmless, skin colour change is reversible), bring contacts for screening.
- **Dispensing vigilance:** check G6PD status before primaquine; pregnancy status before tetracyclines/fluoroquinolones; allergy before penicillins; alcohol warning with metronidazole.
- **Notification:** TB is notifiable — cooperate with NTEP reporting.
- **Prophylaxis advice:** malaria chemoprophylaxis for travellers; deworming schedules for children.
- **Oncology support:** safe handling of cytotoxic drugs, antiemetic counselling, "report fever immediately" education.

3.14 India Context

- **TB:** India's NTEP gives free diagnosis/treatment; pharmacists are treatment supporters and notifiers.
- **Leprosy:** free MDT via NLEP; fight stigma — the cured patient is not infectious.
- **Malaria:** endemic pockets in Odisha, Chhattisgarh, Jharkhand, MP, Northeast; follow the national drug policy (ACT for falciparum).
- **Filariasis & deworming:** mass drug administration (DEC + albendazole) and school National Deworming Day.
- **HIV:** free ART through national programme centres; adherence counselling saves lives.
- **AMR in UTIs/typhoid:** rising resistance makes culture-guided prescribing essential — pharmacists must discourage OTC antibiotic sale (Schedule H1).

3.15 Key Points

1. Antifungals exploit ergosterol (fungal) vs cholesterol (human); amphotericin B is most effective but nephrotoxic.

2. Acyclovir activates only in virus-infected cells — model selective toxicity; HIV always needs triple-drug ART.

3. Albendazole starves worms (microtubule block); DEC + albendazole for filariasis; praziquantel for flukes/tapeworm.

4. Nitrofurantoin concentrates in urine — ideal for cystitis; rising E. coli resistance needs culture guidance.

5. TB: H-R-Z-E first-line; H=liver/nerves, R=red urine + enzyme induction, Z=joints (uric acid), E=eyes; MDR-TB = resistant to H+R, from incomplete treatment.

6. Leprosy: MDT = dapsone + rifampicin + clofazimine; clofazimine colours skin.

7. Malaria: ACT for falciparum (never artemisinin alone); chloroquine + primaquine for vivax; primaquine needs G6PD testing.

8. Amoebiasis: metronidazole (tissue) + diloxanide (lumen); no alcohol with metronidazole.

9. Anticancer drugs have poor selectivity → marrow suppression, vomiting, hair loss; classes: alkylators, antimetabolites, mitotic inhibitors, hormonal, targeted.

10. The combination rule (TB, leprosy, HIV, malaria): multiple drugs, multiple targets = no escape for the germ.

3.16 Common Confusions

Confusion	Clarification
Metronidazole alone cures amoebiasis fully	No — it misses gut cysts; diloxanide furoate must follow for luminal clearance.
Artemisinin alone is enough for falciparum	No — always as ACT; monotherapy breeds resistance.
Orange urine on rifampicin means kidney damage	No — harmless colouring of urine, tears, sweat; warn the patient in advance.
Antibiotics treat viral fevers	No — antibiotics don't act on viruses; misuse drives AMR.
Cancer chemotherapy is highly selective	Opposite — it has the poorest selectivity; that's why side effects are severe.
Stopping TB drugs when feeling better is fine	Dangerous — causes relapse and MDR-TB; full course is mandatory.

3.17 Common Mistakes

1. Writing chloroquine for falciparum malaria as first-line — in resistant areas ACT is first-line.

2. Forgetting G6PD testing before primaquine.

3. Omitting diloxanide after metronidazole in amoebiasis answers.

4. Confusing ethambutol's eye toxicity with isoniazid's nerve toxicity.

5. Listing anticancer adverse effects without explaining why (normal dividing cells hit too).

6. In TB regimens, writing exact months/doses as fixed facts — regimens evolve; state the phase concept and refer to current NTEP guidelines.

3.18 Mnemonics

- **TB first-line:** "**H**urry **R**un, **Z**ap **E**very **S**ickness" (H-R-Z-E-S).
- **TB toxicities:** "**H**urts liver/nerves, **R**ed urine, **Z**aps joints, **E**yes blur."
- **Leprosy MDT:** "**D**apsone, **R**ifampicin, **C**lofazimine."
- **Malaria:** "**V**ivax needs **V**anquish-relapse (primaquine); **F**alciparum needs **F**ast ACT."
- **Amoebiasis:** "**M**etro for **M**eat (tissue), **D**iloxanide for **D**rain (lumen)."
- **Anticancer classes:** "**A**lkylators **A**ttach, **A**ntimetabolites **A**pe, **M**itotic inhibitors **M**angle ropes."

3.19 Exam Summary

Fungal infections are treated with ergosterol-targeting drugs (amphotericin B — nephrotoxic but potent; azoles; echinocandins; terbinafine for skin). Viral infections use selectively activated drugs like acyclovir for herpes and mandatory triple-drug ART for HIV. Helminthiasis is treated with albendazole/mebendazole (microtubule starvation), praziquantel (flukes/tapeworm), ivermectin and DEC (filariasis). UTIs, mostly E. coli, respond to urine-concentrated nitrofurantoin, cotrimoxazole, or fluoroquinolones, with culture guidance amid rising resistance. TB is treated with multidrug first-line therapy (isoniazid, rifampicin, pyrazinamide, ethambutol ± streptomycin) in intensive and continuation phases; incomplete treatment causes MDR-TB (resistance to isoniazid + rifampicin). Leprosy is cured with MDT (dapsone + rifampicin + clofazimine) under NLEP. Malaria treatment is species-based: ACT for P. falciparum (never artemisinin alone) and chloroquine + primaquine (after G6PD testing) for P. vivax. Amoebiasis needs metronidazole for tissue invasion plus diloxanide furoate for luminal cysts, with no alcohol during therapy. Anticancer chemotherapy (alkylating agents, antimetabolites, mitotic inhibitors, hormonal, targeted drugs) suffers poor selectivity, causing marrow suppression, nausea, and hair loss; combination therapy counters resistance as in TB and HIV.

3.20 One-Minute Revision

- Fungi: ergosterol target; ampho B works, harms kidneys.
- Herpes: acyclovir (activates only in infected cells). HIV: always triple ART.
- Worms: albendazole starves; DEC for filaria; prazi for flukes.
- UTI: nitrofurantoin lives in urine; culture if recurrent.
- TB: H-R-Z-E; H liver/nerves, R red urine, Z joints, E eyes; MDR = H+R resistant.
- Leprosy: D+R+C (MDT); clofazimine colours skin.
- Malaria: falciparum → ACT; vivax → chloroquine + primaquine (G6PD check).
- Amoeba: metronidazole + diloxanide; no alcohol.
- Cancer: poor selectivity → marrow/vomiting/hair loss; alkylators, antimetabolites, vincristine, doxorubicin (heart).

3.21 Exam Questions

Short answers

1. Why is amphotericin B both effective and toxic? Explain using ergosterol vs cholesterol.
2. Explain why HIV is always treated with three drugs, never one.
3. What is MDR-TB? How does it develop, and how is it prevented?
4. Why is primaquine added in vivax malaria, and what test is needed before giving it?
5. Explain the two-drug logic in amoebiasis treatment (metronidazole + diloxanide).
6. List the first-line anti-TB drugs with one signature adverse effect each.
7. Why does anticancer chemotherapy cause hair loss and low blood counts?
8. What is the combination rule shared by TB, leprosy, HIV, and malaria treatment?

Long answers

1. Discuss the chemotherapy of tuberculosis: causative agent characteristics, first-line drugs with mechanisms and adverse effects, the rationale of multidrug therapy, and the concept of MDR-TB. Add India's NTEP context.

2. Describe the chemotherapy of malaria: species differences, drug choices for vivax and falciparum with mechanisms, the role of primaquine and ACTs, and resistance considerations.

3. Classify anticancer drugs with examples. Explain why their selectivity is poor and describe their common adverse effects.

4. Write notes on: (a) drugs for fungal infections, (b) drugs for helminthiasis, (c) drugs for UTI — covering key drugs, why they are chosen, and major adverse effects.

MCQs

1. Amphotericin B acts by:

a) Blocking ergosterol synthesis b) Binding ergosterol and punching holes in the fungal membrane c) Blocking fungal cell-wall synthesis d) Inhibiting DNA gyrase

1. Acyclovir's selectivity comes from:

a) Blocking human DNA polymerase b) Activation only in virus-infected cells by viral thymidine kinase c) Destroying the virus outside cells d) Boosting immunity

1. MDR-TB is defined as resistance to at least:

a) Streptomycin and ethambutol b) Isoniazid and rifampicin c) Pyrazinamide and ethambutol d) Any two antibiotics

1. Orange-red urine during TB treatment is caused by:

a) Isoniazid b) Rifampicin (harmless) c) Pyrazinamide d) Ethambutol

1. Optic neuritis (vision/colour disturbance) in TB therapy is caused by:

a) Rifampicin b) Ethambutol c) Isoniazid d) Streptomycin

1. Primaquine is essential in vivax malaria to:

a) Kill blood-stage parasites fast b) Kill dormant liver stages and prevent relapse c) Prevent mosquito bites d) Treat cerebral malaria

1. Before giving primaquine, one must check:

a) Blood sugar b) G6PD status c) Liver biopsy d) ECG

1. Clofazimine's characteristic side effect:

a) Reddish-brown skin discolouration b) Tendon rupture c) Grey baby syndrome d) Orange urine

1. Metronidazole + alcohol causes:

a) No interaction b) Disulfiram-like reaction c) Increased cure rate d) Orange urine

1. Doxorubicin's dose-limiting toxicity:

a) Kidney damage b) Cardiotoxicity (heart damage) c) Tendon rupture d) Teeth staining

1. Nitrofurantoin is ideal for cystitis because it:

a) Concentrates in urine b) Crosses the blood-brain barrier c) Kills viruses d) Is given as a single injection

1. Albendazole kills worms by:

a) Paralyzing nerves b) Blocking microtubules so the worm starves c) Dissolving the worm's skin d) Blocking DNA gyrase

Answer key: 1-b, 2-b, 3-b, 4-b, 5-b, 6-b, 7-b, 8-a, 9-b, 10-b, 11-a, 12-b.

Viva questions (with answers)

1. Q: Why is TB treatment given for months, not days?

A: M. tuberculosis grows very slowly and hides inside cells behind a waxy wall; long multidrug therapy is needed to kill all bacilli including dormant ones and prevent resistance.

1. **Q: A TB patient complains his tears stain his contact lenses orange. What do you tell him?**

A: It is rifampicin — harmless colouring of urine, tears, sweat, and saliva; continue the medicine and avoid soft contact lenses during treatment.

1. **Q: Why can't we use a single drug for leprosy?**

A: Single-drug (dapsone) therapy bred resistant M. leprae; MDT with three drugs prevents resistance and cures faster.

1. **Q: Name the drug of choice for amoebic liver abscess and its alcohol warning.**

A: Metronidazole; no alcohol during treatment (disulfiram-like reaction) plus metallic taste.

1. **Q: Which antimalarial kills the dormant liver stages of vivax, and what is its danger?**

A: Primaquine; danger is haemolysis in G6PD-deficient patients — test first.

1. **Q: Why do cancer patients lose hair during chemotherapy?**

A: Anticancer drugs attack all rapidly dividing cells, including hair-root cells — poor selectivity.

Application-based questions

1. A TB patient stops medicines after 2 months feeling cured; 6 months later sputum shows resistance to isoniazid and rifampicin. Explain the microbiology of what happened and outline the principles of his further management (no exact regimen needed).

2. A pregnant woman in her first trimester has an uncomplicated UTI. Her urine culture shows E. coli sensitive to nitrofurantoin, cotrimoxazole, and ciprofloxacin. Which would you recommend and why? Which would you avoid?

3. A traveller to a forested district of Odisha asks for malaria prevention. Explain chemoprophylaxis options and mosquito-bite precautions you would advise as a pharmacist.

3.22 References

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