

Rifamycins

Bactericidal inhibitors of bacterial DNA-dependent RNA polymerase, anchoring first-line tuberculosis therapy and defined clinically by CYP450 induction, orange secretions and single-step rpoB resistance.

Online guide: <https://www.medguideglobal.com/pharmacology/antibiotics/rifamycins>

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Quick revision

One Liner: Rifamycins inhibit bacterial DNA-dependent RNA polymerase and kill the organism by arresting RNA synthesis - first-line for tuberculosis but only ever in combination, because a single rpoB mutation is enough to defeat them.

1. Mechanism: inhibit bacterial DNA-dependent RNA polymerase, sterically obstructing the path of the elongating RNA and arresting RNA synthesis. [1]
2. The effect is bactericidal, and the target is unique to microbial RNA polymerase rather than the human enzyme. [1]
3. Rifampin is paired with other antimicrobial agents to avert drug resistance - monotherapy selects resistant mutants. [1]
4. Resistance is overwhelmingly due to mutations in the rpoB gene encoding the RNA polymerase beta subunit. [5]
5. Rifampin induces CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2, diminishing the effectiveness of oral contraceptives, warfarin and protease inhibitors. [1]
6. Orange discoloration of tears, sweat, saliva, urine and feces is a dose-dependent, harmless but alarming class signature. [1]
7. Flu-like symptoms are a dose-independent hypersensitivity reaction, more frequent when rifampin is given intermittently or over an extended period. [1]
8. Rifabutin is a far weaker enzyme inducer than rifampin (relative induction potency about 0.4 versus 1.0), which is why it substitutes for rifampin in patients on interaction-sensitive drugs such as antiretrovirals. [3]
9. Rifaximin is essentially non-absorbed (under 0.4% reaches blood or urine), confining its action to the gut lumen. [2]

Overview

1. Rifamycins are bactericidal antibiotics that inhibit bacterial DNA-dependent RNA polymerase, uniquely targeting the microbial enzyme and arresting ongoing RNA synthesis. Rifampin (rifampicin), the prototype, is active against a wide range of gram-positive organisms including mycobacteria and *Clostridium difficile*, and against specific gram-negative organisms including *Neisseria meningitidis*, *N. gonorrhoeae* and *Haemophilus influenzae*. [1]
2. The class's defining clinical role is tuberculosis, where rifampin anchors combination regimens and is deliberately never used alone - resistance emerges readily through mutation of the rpoB gene, which accounts for the overwhelming majority of rifampin-resistant *Mycobacterium tuberculosis* isolates. The other members are variations on the rifampin theme: rifapentine has a longer half-life allowing once- or twice-weekly dosing in tuberculosis regimens, rifabutin trades induction potency for compatibility with antiretrovirals in HIV care, and rifaximin abandons systemic absorption altogether to work purely in the gut lumen. [1][5][4][3][2]
3. What makes the class demanding in practice is pharmacology rather than spectrum. Rifampin is a potent inducer of CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2, diminishing the effectiveness of co-administered oral contraceptives, warfarin and protease inhibitors; it turns body fluids orange in a dose-dependent way; hepatotoxicity is a recognized risk, particularly with pre-existing liver disease; and intermittent or prolonged administration makes hypersensitivity-type flu-like reactions more frequent. [1]

Classification and drug examples

Intro: Best learned by how each member modifies the rifampin template: potency of enzyme induction, half-life, and whether the drug is absorbed at all.

1. Name: Systemic first-line antitubercular rifamycins

1. Note: Rifampin is the prototype and strongest CYP inducer; rifapentine's longer half-life allows once- or twice-weekly dosing in tuberculosis regimens.

1. Name: Rifampin

Rifampicin

1. Route: Oral/IV

1. Note: Anchor of tuberculosis combination therapy; also used in latent tuberculosis, leprosy (off-label) and elimination of meningococcal carriage. [1]

2. Name: Rifapentine

2. Route: Oral

2. Note: Longer half-life than rifampin and rifabutin, allowing once- or twice-weekly dosing; used with isoniazid in latent tuberculosis regimens. Induction potency sits between rifabutin and rifampin. [4] [1][4]

2. Name: Less-inducing rifamycin for HIV co-therapy

2. Note: Chosen when P450-sensitive co-medication, especially antiretroviral therapy, makes rifampin's induction unacceptable.

Name: Rifabutin

Route: Oral

Note: Used largely to prevent Mycobacterium avium complex disease in advanced HIV infection; far weaker enzyme inducer than rifampin (about 0.4 versus 1.0); rare but severe uveitis is its characteristic adverse effect. [3] [3]

3. Name: Non-absorbed luminal rifamycin

3. Note: Systemic exposure is engineered out, confining both effect and toxicity to the gastrointestinal tract.

Name: Rifaximin

Route: Oral

Note: Under 0.4% detectable in blood or urine; approved for travelers' diarrhea from noninvasive E. coli, reduction of overt hepatic encephalopathy recurrence, and IBS-D. [2] [2]

Mechanism of action

Summary: Rifamycins bind bacterial DNA-dependent RNA polymerase and sterically obstruct the path of the elongating RNA, arresting RNA synthesis and killing the organism. The target is unique to the microbial enzyme, sparing human RNA polymerase.

Target: Bacterial DNA-dependent RNA polymerase (beta subunit, encoded by rpoB)

Cidal Static: bactericidal

Kill Kinetics: see prescribing reference

1. Step: 1

1. Title: The drug reaches the bacterial RNA polymerase

1. Detail: Rifamycins act on the microbial DNA-dependent RNA polymerase, a target human cells do not share in inhibitable form - the basis of their selective toxicity. [1]

2. Step: 2

2. Title: It binds the polymerase and blocks the RNA exit path

2. Detail: Binding sterically obstructs the path of the elongating RNA transcript. [1]

3. Step: 3

3. Title: Ongoing RNA synthesis is arrested

3. Detail: With transcription stopped, the organism can no longer make the messenger RNA that all downstream

protein synthesis depends on. [1]

4. Step: 4

4. Title: The organism dies

4. Detail: The effect is bactericidal - transcription arrest is lethal, not merely growth-suppressing. [1]

5. Step: 5

5. Title: A mutated rpoB polymerase escapes the drug

5. Detail: Point mutations in the rpoB gene alter the beta subunit so the drug no longer binds effectively - the single-step resistance mechanism that forbids monotherapy in tuberculosis. [5][1]

Spectrum of activity

Intro: Rifampin defines the systemic spectrum; rifaximin applies rifamycin chemistry to gut flora only.

1. Subclass Id: systemic-antitubercular

1. Wide range of gram-positive cocci

2. Clostridium difficile

1. Neisseria meningitidis

2. Neisseria gonorrhoeae

3. Haemophilus influenzae

1. Mycobacterium tuberculosis

2. Mycobacterium leprae (off-label leprosy use)

1. Most enteric gram-negative bacilli as monotherapy

2. Any organism once rpoB mutation is established [1][5]

2. Subclass Id: hiv-adapted

Mycobacterium avium complex (prevention in advanced HIV)

Isolates carrying rpoB mutations that confer rifabutin cross-resistance [3][5]

3. Subclass Id: non-absorbed-luminal

Gram-positive aerobic and anaerobic gut flora

1. Gram-negative aerobic and anaerobic gut flora

2. Noninvasive strains of Escherichia coli

Luminal anaerobes

1. Any infection outside the gastrointestinal lumen

2. Invasive or febrile dysenteric diarrhea [2]

Major clinical uses

1. Drug: Rifampin

1. Organism: Mycobacterium tuberculosis

1. Indication: Active tuberculosis, always within combination regimens

1. Line: first-line

1. Note: Paired with other antimicrobial agents specifically to avert resistance. [1]

2. Drug: Rifampin

2. Organism: Mycobacterium tuberculosis (latent)

2. Indication: Latent tuberculosis infection

2. Line: first-line

2. Note: Regimen selection belongs to a prescribing reference and treating clinician. [1]

3. Drug: Rifampin

3. Organism: Neisseria meningitidis

3. Indication: Elimination of meningococcal carriage in asymptomatic carriers

3. Line: targeted

3. Note: A prophylactic, not a treatment for invasive meningococcal disease. [1]
4. Drug: Rifampin
4. Organism: Mycobacterium leprae
4. Indication: Leprosy (off-label), within multidrug regimens
4. Line: targeted
4. Note: Off-label use documented in the class reference. [1]
5. Drug: Rifapentine
5. Organism: Mycobacterium tuberculosis (latent)
5. Indication: Once-weekly latent tuberculosis therapy in combination with isoniazid
5. Line: first-line
5. Note: The long half-life is what makes weekly dosing possible. [4]
6. Drug: Rifabutin
6. Organism: Mycobacterium avium complex
6. Indication: Prevention of MAC disease in advanced HIV infection
6. Line: targeted
6. Note: Preferred over rifampin when antiretrovirals or other P450-sensitive drugs are on board. [3]
7. Drug: Rifaximin
7. Organism: Noninvasive strains of Escherichia coli
7. Indication: Travelers' diarrhea
7. Line: targeted
7. Note: Approved for noninvasive E. coli; not for invasive, febrile dysenteric illness. [2]
8. Drug: Rifaximin
8. Organism: Ammonia-producing gut flora
8. Indication: Reduction in risk of overt hepatic encephalopathy recurrence in adults
8. Line: adjunct
8. Note: Luminal action with very low systemic exposure suits patients with advanced liver disease. [2]
9. Drug: Rifaximin
9. Organism: Gut flora
9. Indication: Irritable bowel syndrome with diarrhea (IBS-D) in adults
9. Line: targeted
9. Note: An FDA-approved indication of the non-absorbed member only. [2]

Pharmacokinetics

1. Drug: Rifampin
1. Route: Oral/IV
1. Absorption: Well absorbed for systemic therapy
1. Csf Penetration: Used in mycobacterial and meningococcal indications under specialist direction
1. Metabolism: Extensive hepatic metabolism; potent inducer of CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2, including induction of its own metabolism
1. Elimination: Biliary and renal
1. Half Life: See prescribing reference
1. Dose Adjust: Caution and monitoring in hepatic impairment [1]
2. Drug: Rifapentine
2. Route: Oral
2. Absorption: Absorbed for systemic therapy
2. Csf Penetration: See prescribing reference
2. Metabolism: Hepatic; induction potency intermediate between rifabutin and rifampin

2. Elimination: See prescribing reference
2. Half Life: Longer than rifampin and rifabutin, permitting once- or twice-weekly dosing
2. Dose Adjust: See prescribing reference [4]
3. Drug: Rifabutin
3. Route: Oral
3. Absorption: Absorbed for systemic therapy
3. Csf Penetration: See prescribing reference
3. Metabolism: Hepatic; far less P450 induction than rifampin (relative potency about 0.4)
3. Elimination: See prescribing reference
3. Half Life: See prescribing reference
3. Dose Adjust: Interacting antiretrovirals may require adjustment per prescribing reference [3]
4. Drug: Rifaximin
4. Route: Oral
4. Absorption: Essentially non-absorbed - under 0.4% detectable in blood or urine
4. Csf Penetration: Not applicable
4. Metabolism: Minimal systemic exposure by design
4. Elimination: Faecal
4. Half Life: Not clinically relevant systemically
4. Dose Adjust: See prescribing reference [2]
1. Enzyme induction is the pharmacokinetic axis of the class: rifampin is the reference inducer, rifapentine is intermediate, and rifabutin is the weakest - the ranking that decides which rifamycin a patient on antiretrovirals, warfarin or hormonal contraception can safely receive. [3][4][1]
2. Rifaximin inverts the class logic: instead of maximizing systemic exposure it eliminates it, achieving high gastrointestinal luminal concentrations with very low blood levels. [2]
3. This page gives no dose regimens by design. Doses depend on indication, regimen phase, weight, hepatic function and co-medication, and belong in a prescribing reference used by the treating clinician.

Adverse effects

1. Effect: Orange-red discoloration of body fluids
1. Detail: Dose-dependent discoloration of tears, sweat, saliva, urine and feces. Harmless, but patients must be warned in advance. [1]
2. Effect: Gastrointestinal upset
2. Detail: Nausea and gastrointestinal disturbance are among the recognized dose-related effects of rifampin therapy. [1]
1. Effect: Hepatotoxicity
1. Detail: A recognized risk of rifampin, particularly in individuals with existing liver conditions.
1. Action: Monitor liver enzymes and symptoms of liver disease during therapy; reassess the regimen if injury develops. [1]
2. Effect: Hypersensitivity reactions including flu-like syndrome
2. Detail: Dose-independent reactions - flu-like symptoms, thrombocytopenia, hemolysis and renal failure - are frequent when rifampin is administered intermittently or over an extended period.
2. Action: Recognize the pattern, review dosing continuity, and escalate rather than rechallenging blindly. [1]
3. Effect: Uveitis (rifabutin)
3. Detail: A rare but potentially severe adverse event specific to rifabutin.
3. Action: Take new eye pain, redness or visual change in a rifabutin-treated patient seriously and arrange ophthalmic assessment. [3]
1. Drug: Rifampin

1. Effect: Strongest enzyme inducer of the class; hepatotoxicity risk concentrates here, especially with pre-existing liver disease. [1]
2. Drug: Rifabutin
2. Effect: Minor transient aminotransferase elevations in a small proportion of patients; uveitis and orange discoloration of urine and sweat; clinically apparent liver injury has not been clearly reported. [3]
3. Drug: Rifapentine
3. Effect: Minor transient aminotransferase elevations in 2 to 7% of patients on long-term therapy; routine monitoring for symptoms of liver disease is recommended for all regimens. [4]
4. Drug: Rifaximin
4. Effect: Adverse effects are largely confined to the gut because systemic absorption is minimal. [2]

Contraindications, precautions and interactions

1. Hypersensitivity to rifampin or other rifamycins. [1]
2. Rifampin co-administration with protease inhibitors, whose concentrations it can lower to failure. [1]
1. Existing liver disease - hepatotoxicity risk is higher, and liver monitoring is part of therapy. [1]
2. Intermittent or interrupted dosing patterns, which make hypersensitivity-type reactions more frequent. [1]
1. With: Combined oral contraceptives
1. Effect: Enzyme induction diminishes contraceptive effectiveness - unplanned pregnancy is the exam-classic consequence; alternative or additional contraception is needed. [1]
2. With: Warfarin
2. Effect: Induction of its metabolizing enzymes reduces anticoagulant effect. [1]
3. With: Protease inhibitors and other antiretrovirals
3. Effect: Rifampin can lower their concentrations; rifabutin, a far weaker inducer, is the usual substitute in HIV co-therapy. [1][3]
4. With: Substrates of CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2 generally
4. Effect: Rifampin induction diminishes the effectiveness of a wide range of concurrently administered drugs; every co-medication needs an interaction check. [1]

Resistance mechanisms

1. Mechanism: rpoB target mutation
1. Detail: The overwhelming majority of rifampin-resistant Mycobacterium tuberculosis isolates carry point mutations in rpoB, the gene encoding the RNA polymerase beta subunit, so the drug can no longer bind its target. This single-step mechanism is why monotherapy is forbidden.
- Rifampin-resistant Mycobacterium tuberculosis
1. Countermeasure: Always use combination regimens; confirm susceptibility and manage resistant disease under specialist care. [5][1]
2. Mechanism: Variable cross-resistance within the class
2. Detail: Cross-resistance between rifampin and rifabutin is common but mutation-dependent: certain rpoB mutations confer rifampin resistance while leaving the isolate rifabutin-susceptible.
- Rifampin-resistant, rifabutin-susceptible M. tuberculosis isolates
2. Countermeasure: Mutation-level susceptibility testing before assuming the whole class is lost. [5]
3. Mechanism: Progressive resistance in non-mycobacterial use
3. Detail: Bacterial resistance to rifampin is progressively more prevalent, and staphylococci in particular develop resistance when it is used without a companion agent.
- MRSA strains developing rifampin resistance
3. Countermeasure: Reserve rifampin for combination use guided by susceptibility data. [1]
- Stewardship Note: The stewardship rule for this class is structural: a single rpoB point mutation defeats every systemic

rifamycin to a varying degree, so rifampin is never given alone for tuberculosis, and any temptation to use it as convenient monotherapy elsewhere spends a first-line antitubercular for a trivial gain.

Comparison tables

Title: The four rifamycins at a glance

Caption: One mechanism, four deployment strategies. Local guidelines and a prescribing reference govern actual therapy.

1. Key: drug

1. Label: Drug

1. Is Row Header: true

2. Key: niche

2. Label: Clinical niche

3. Key: induction

3. Label: CYP450 induction

4. Key: distinctive

4. Label: Distinctive point

1. Drug: Rifampin (rifampicin)

1. Niche: First-line tuberculosis combinations; latent TB; meningococcal carriage; leprosy (off-label)

1. Induction: Strongest (reference potency 1.0)

1. Distinctive: Orange secretions; hepatotoxicity; the classic interaction drug [1][3]

2. Drug: Rifapentine

2. Niche: Once-weekly latent TB therapy with isoniazid; TB combinations

2. Induction: Intermediate between rifabutin and rifampin

2. Distinctive: Longest half-life of the class, enabling weekly dosing [4]

3. Drug: Rifabutin

3. Niche: MAC prevention in advanced HIV; rifampin substitute with antiretrovirals

3. Induction: Weakest (about 0.4 relative to rifampin)

3. Distinctive: Uveitis is its signature rare toxicity [3]

4. Drug: Rifaximin

4. Niche: Travelers' diarrhea; hepatic encephalopathy recurrence; IBS-D

4. Induction: Not clinically relevant - essentially no systemic exposure

4. Distinctive: Under 0.4% absorbed; acts only in the gut lumen [2]

High-yield exam pearls

1. Pearl: Rifamycins are the only major class that switches off bacterial transcription.

1. Why: They inhibit DNA-dependent RNA polymerase and arrest ongoing RNA synthesis, a target no other first-line antitubercular shares - and the microbial enzyme is targeted selectively over the human one. [1]

2. Pearl: Never alone in tuberculosis - one rpoB point mutation defeats the drug.

2. Why: Rifampin is deliberately paired with other agents to avert resistance, because the great majority of rifampin-resistant Mycobacterium tuberculosis isolates carry rpoB mutations that arise readily under monotherapy. [1][5]

3. Pearl: Rifampin is the classic exam CYP inducer.

3. Why: It induces CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2, so oral contraceptives fail, warfarin anticoagulation falls, and protease inhibitor concentrations drop - the standard three-way interaction stem. [1]

4. Pearl: Orange-red secretions identify the drug in one line.

4. Why: Dose-dependent orange discoloration of tears, sweat, saliva, urine and feces is harmless but must be counselled - it can stain soft contact lenses and frightens uninformed patients. [1]

5. Pearl: Flu-like syndrome points to intermittent dosing.
5. Why: The dose-independent hypersensitivity reactions of rifampin - flu-like symptoms, thrombocytopenia, hemolysis, renal failure - are frequent when the drug is administered intermittently or over an extended period. [1]
6. Pearl: Rifabutin is the rifamycin for HIV co-therapy; uveitis is its own trap.
6. Why: It is used largely to prevent Mycobacterium avium complex disease in advanced HIV and induces P450 enzymes far less than rifampin, but carries a rare risk of uveitis. [3]
7. Pearl: Rifaximin stays in the gut on purpose.
7. Why: Its non-absorbable profile gives high luminal concentrations with very low systemic levels, which is exactly why it works for travelers' diarrhea, hepatic encephalopathy recurrence and IBS-D. [2]

Common exam traps

1. Trap: "Rifampin inhibits protein synthesis."
1. Correction: Rifampin inhibits DNA-dependent RNA polymerase - transcription, not translation. Protein synthesis inhibitors act on the ribosome; rifamycins act one step upstream. [1]
2. Trap: "Orange urine on rifampin means liver damage or hematuria."
2. Correction: Orange discoloration of body fluids is a dose-dependent, expected effect of the drug itself. Hepatotoxicity is a separate, real risk that is tracked with liver enzymes, not urine color. [1]
3. Trap: "All rifamycins interact equally with antiretrovirals."
3. Correction: Rifampin is the strongest inducer and can lower protease inhibitor concentrations enough to be contraindicated; rifabutin's induction potency is roughly 0.4 relative to rifampin's 1.0, which is why it is the substitute in HIV co-therapy. [1][3]
4. Trap: "Rifaximin treats systemic infection like the other rifamycins."
4. Correction: Rifaximin is essentially non-absorbed - under 0.4% is detectable in blood or urine - so its role is confined to the gastrointestinal lumen: travelers' diarrhea from noninvasive E. coli, hepatic encephalopathy recurrence and IBS-D. [2]
5. Trap: "Rifampin resistance always means rifabutin is useless too."
5. Correction: Cross-resistance is common but not universal: some rpoB mutations confer rifampin resistance while the isolate remains rifabutin-susceptible. [5]

Self-test questions

1. Question: A student writes that rifampin works by inhibiting bacterial protein synthesis. What is the correct mechanism?
 1. Inhibition of the 50S ribosomal subunit, blocking peptide bond formation
 2. Inhibition of bacterial DNA-dependent RNA polymerase, arresting transcription
 3. Inhibition of DNA gyrase, preventing supercoiling of the chromosome
 4. Inhibition of dihydropteroate synthase, blocking folate synthesis
1. Explanation: The drug binds the microbial DNA-dependent RNA polymerase and sterically obstructs the path of the elongating transcript, so RNA synthesis halts. That is transcription rather than translation, one step upstream of where the ribosomal agents work. The enzyme attacked is the bacterial one, which is why the human polymerase is spared, and the arrest kills rather than merely suppressing growth. [1]
2. Question: Why is rifampin deliberately never given alone for active tuberculosis?
 1. Given alone it is only bacteriostatic and cannot clear the organism
 2. Monotherapy causes unacceptable orange discoloration of body fluids
 3. It has no activity against Mycobacterium tuberculosis without a companion drug
 4. Resistance is a single-step event: rpoB point mutations account for the overwhelming majority of resistant isolates
2. Explanation: The rpoB gene encodes the beta subunit of RNA polymerase, and a point mutation there reshapes the binding site so the drug no longer attaches. Nearly every resistant Mycobacterium tuberculosis isolate carries such a

mutation, and monotherapy is precisely the condition that selects for it, so companion agents are built into the regimen to avert that outcome. [5][1]

3. Question: A woman taking a combined oral contraceptive starts rifampin and is told she needs additional contraception. What underlies that advice?

1. Rifampin potently induces CYP3A4 and several other P450 enzymes, accelerating clearance of co-administered drugs

2. Rifampin inhibits CYP3A4, causing hormone accumulation and receptor downregulation

3. Rifampin displaces the hormones from plasma protein binding sites

4. Rifampin binds the contraceptive in the gut and prevents its absorption

3. Explanation: Induction of CYP3A4, CYP2C9, CYP2C19, CYP2C8 and CYP1A2 speeds the metabolism of a wide range of co-medications, so their effect falls away. Contraceptive failure, weakened warfarin anticoagulation and falling protease inhibitor concentrations are the three consequences worth committing to memory, and every concurrent drug deserves an interaction check. [1]

4. Question: A patient two weeks into rifampin therapy reports orange tears and urine. What is the correct interpretation?

1. Early hepatotoxicity, best confirmed by repeating the urine colour

2. Haematuria from drug-induced interstitial nephritis

3. An expected, dose-dependent and harmless property of the drug itself

4. A hypersensitivity reaction requiring immediate withdrawal

4. Explanation: Tears, sweat, saliva, urine and faeces all take on the colour, its intensity tracks the dose, and no harm follows. Warning the patient in advance is what matters, since soft contact lenses can be stained and an uncounselled patient may abandon treatment over it. Liver injury is a genuinely separate risk, tracked with liver enzymes rather than by the colour of urine. [1]

5. Question: Why is rifabutin, rather than rifampin, generally selected for a patient receiving antiretroviral therapy?

1. Rifabutin is bactericidal whereas rifampin is only bacteriostatic against mycobacteria

2. Rifabutin induces P450 enzymes far more weakly, with a relative potency around 0.4 against rifampin at 1.0

3. Rifabutin is not absorbed systemically, so no interaction is possible

4. Rifabutin has no known serious adverse effects

5. Explanation: Rifampin is the strongest inducer of the family and can drive protease inhibitor concentrations down far enough for the pairing to be contraindicated. Its weaker relative sits at roughly 0.4 on that same scale, which is what makes it the substitute in HIV care, where it is used largely to prevent Mycobacterium avium complex disease. It is not free of hazard, though, since uveitis is its rare but potentially severe signature. [3][1]

6. Question: Rifaximin is a rifamycin, yet it has no role in tuberculosis or any other systemic infection. Why?

1. Its target is a fungal rather than a bacterial enzyme

2. It is inactivated by first-pass hepatic metabolism before reaching the circulation

3. Mycobacteria are intrinsically resistant to it through efflux

4. It is essentially non-absorbed, with under 0.4% detectable in blood or urine, so it acts only in the gut lumen

6. Explanation: Non-absorption is engineered rather than accidental: luminal concentrations run high while blood levels stay negligible. That is precisely why its approved uses are all gastrointestinal, covering travellers diarrhoea caused by noninvasive Escherichia coli, reduction of overt hepatic encephalopathy recurrence, and irritable bowel syndrome with diarrhoea, and why invasive febrile dysenteric illness falls outside its remit. [2]

7. Question: Flu-like symptoms with thrombocytopenia develop in a patient receiving rifampin on an intermittent schedule. How is this best characterised?

1. A dose-dependent toxic effect that settles if the dose is lowered

2. An expected consequence of enzyme induction acting on cytokine metabolism

3. A dose-independent hypersensitivity reaction, more frequent with intermittent or prolonged administration

4. Early hepatotoxicity, which always presents in this way

7. Explanation: This family of reactions does not track the dose at all. Flu-like symptoms sit alongside thrombocytopenia, haemolysis and renal failure in the same hypersensitivity group, and they become commoner when the drug is given in an interrupted pattern or carried on over an extended period. Recognising the pattern and escalating, rather than rechallenging blindly, is the point being examined. [1]

8. Question: Which property allows rifapentine to be used on a once-weekly schedule with isoniazid in latent tuberculosis?

1. A half-life longer than that of rifampin and rifabutin
2. Complete absence of cytochrome P450 induction
3. Restriction of its distribution to the gastrointestinal lumen
4. Conversion in the liver into a long-lasting active metabolite of rifampin

8. Explanation: It outlasts the other members of the family in the body, and that alone is the basis for once- or twice-weekly administration in tuberculosis regimens. On enzyme induction it is not innocent either, since its potency lies between rifabutin and rifampin. Minor transient aminotransferase rises are reported in 2 to 7% of patients on long-term therapy. [4]

Frequently asked questions

1. Question: Why is rifampin never used alone for tuberculosis?

1. Answer: Because resistance is a single-step event: point mutations in the *rpoB* gene, found in the overwhelming majority of rifampin-resistant isolates, stop the drug binding its RNA polymerase target. Combination therapy exists specifically to avert that selection. [1][5]

2. Question: Is the orange discoloration of urine and tears on rifampin dangerous?

2. Answer: No - it is a dose-dependent property of the drug itself, affecting tears, sweat, saliva, urine and feces, and it is harmless. It matters only because uncounselled patients stop treatment over it. [1]

3. Question: Why does rifampin cause oral contraceptive failure?

3. Answer: It is a potent inducer of cytochrome P450 enzymes including CYP3A4, so co-administered drugs are metabolized faster and lose effect. Contraceptives, warfarin and protease inhibitors are the three interactions worth memorizing. [1]

4. Question: When is rifabutin chosen over rifampin?

4. Answer: Mainly in HIV care - for preventing *Mycobacterium avium* complex disease in advanced infection, and as the rifamycin of choice when antiretrovirals or other P450-sensitive drugs are on board, because its enzyme induction is far weaker than rifampin's. [3]

5. Question: How can rifaximin be an antibiotic that is not absorbed?

5. Answer: Non-absorption is the design: under 0.4% reaches blood or urine, so the drug concentrates in the gastrointestinal lumen. That is why its approved uses - travelers' diarrhea from noninvasive *E. coli*, hepatic encephalopathy recurrence and IBS-D - are all gut conditions. [2]

6. Question: What is the flu-like syndrome with rifampin?

6. Answer: A dose-independent hypersensitivity reaction - flu-like symptoms that can accompany thrombocytopenia, hemolysis and renal failure - that becomes more frequent when rifampin is given intermittently or over an extended period. [1]

References

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