

Tuberculosis

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THE STORY IN ONE SENTENCE

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“Tuberculosis is a chronic infection where the body walls off bacteria but cannot kill them. Active disease needs isolation and four drugs together (RIPE: rifampin, isoniazid, pyrazinamide, ethambutol) for at least six months.”

Normal anatomy — the body's job

Alveolar macrophages (cleanup cells in the tiny air sacs of the lungs) normally capture and kill breathed-in bacteria. When M. tuberculosis is inhaled, macrophages eat the bacteria and build granulomas—tiny walled-off bunkers made of immune cells—to trap any bacteria they cannot kill. The bacteria stay alive but dormant inside these granulomas, and you feel healthy. This balance is called latent TB, and about 90% of infected people stay in this latent state for life.

BODY'S JOB

The alveolar macrophages' job is to patrol the air sacs (alveoli) where oxygen crosses into the blood, swallow any invading germs, and destroy them with acid and enzymes. If a germ is too tough to kill, the body calls in more immune cells to surround it and build a granuloma—a tiny fortress that seals the germ off from healthy tissue. This keeps the infection from spreading while your immune system stays on guard.

1. You breathe in tiny droplets carrying M. tuberculosis bacteria from someone with active TB who coughs or sneezes.
2. The bacteria land in the alveoli (air sacs deep in the lungs where oxygen enters the blood).
3. Alveolar macrophages (the lung's cleanup crew) swallow the bacteria and try to kill them with acid and enzymes.
4. M. tuberculosis has a waxy coat that resists the acid, so the bacteria survive inside the macrophages.

5. The body sends more immune cells (T cells and more macrophages) to surround the infected macrophages and build a granuloma—a walled-off pocket that traps the bacteria.
6. The bacteria stay alive but dormant inside the granuloma. You have no symptoms. This is latent TB.
7. Your immune system keeps the granuloma walls strong, and the bacteria stay locked in for years or even your whole life.

What breaks

The break is that macrophages cannot kill *M. tuberculosis* because the bacteria have a thick, waxy coat (made of mycolic acid) that protects them from the acid and enzymes inside the macrophage. Instead of dying, the bacteria multiply slowly inside the macrophages. The body builds granulomas to trap them, but the granulomas only contain the bacteria—they do not kill them. If your immune system weakens, the granuloma walls crumble, the bacteria escape and multiply, and you get active TB.

CLINICAL TERM

Alveolar macrophages phagocytose *M. tuberculosis* but cannot kill it because the bacteria's mycolic acid-rich cell wall resists lysosomal enzymes and acidic pH. The bacteria replicate intracellularly. CD4+ T helper cells and macrophages form caseating granulomas (organized collections of immune cells with a dead (necrotic) center) to contain the bacteria, establishing latent TB infection. Reactivation occurs when cell-mediated immunity (especially CD4+ T cell function) declines, allowing bacterial replication and tissue destruction.

How the body compensates

The body tries to limit damage by walling off bacteria in granulomas and ramping up inflammation (fever, night sweats, weight loss). Vital signs can look normal for weeks or months while the infection smolders, but the body is burning energy and losing ground. The danger is missing the slow slide toward the crash point: meningitis, miliary (widespread) TB, or cavitary lung disease with severe bleeding.

1. {'step': 'Granuloma formation traps bacteria', 'why': 'Macrophages and T cells surround the bacteria and build a granuloma—a walled pocket—so the bacteria cannot spread to healthy tissue. This buys time but does not cure the infection.'}

2. {'step': 'Inflammation runs constantly', 'why': 'The immune system releases cytokines (inflammatory signals like TNF-alpha and interferon-gamma) to keep the granuloma walls tight. This causes fever (the body raising its thermostat to slow bacterial growth), night sweats (the fever breaking overnight), and weight loss (the body burning extra calories to fuel the immune response).'}
3. {'step': 'Cough expels infected tissue', 'why': 'As bacteria multiply and damage lung air sacs, the lungs produce mucus and the body coughs to clear the infected material. This spreads bacteria to others but also reduces the bacterial load in the lungs.'}
4. {'step': 'Vital signs stay normal early on', 'why': 'Blood pressure, heart rate, and oxygen levels remain stable because the infection is localized in the lungs and the body compensates. This is the dangerous middle—patients look stable but are slowly getting worse.'}
5. {'step': 'Watch for the crash point before it arrives', 'why': 'The crash happens when granulomas break down completely (cavitary disease with massive coughing up blood (hemoptysis)—coughing up large amounts of blood), bacteria flood the bloodstream (miliary TB—tiny seed-like spots throughout the lungs and other organs), or infection spreads to the brain (TB meningitis—headache, stiff neck, confusion, seizures). Once the crash starts, the window to save the patient narrows fast.'}
6. {'step': 'Track trends, not single snapshots', 'why': 'A patient with stable vitals today but three weeks of worsening cough, worsening weight loss, and rising fever is on a downhill slope. Do not wait for the vitals to crash—act on the pattern.'}

Domino effect

1. Macrophages cannot kill *M. tuberculosis* — The bacteria's waxy coat (mycolic acid) protects it from the acid and enzymes inside alveolar macrophages, so the bacteria survive and multiply slowly inside the cells instead of dying.
2. Granulomas form to trap bacteria but cannot kill them — The body sends CD4+ T cells and more macrophages to surround infected macrophages and build a granuloma—a walled pocket with a dead, cheesy center (caseous tissue death (necrosis)). This stops bacteria from spreading but keeps them alive inside the walls. Most people stay in this latent state for life.
3. Weakened immunity lets bacteria escape and multiply — If CD4+ T cell function drops (HIV, TNF-alpha blockers, steroids, diabetes, malnutrition, very young or old age), the granuloma walls crumble, bacteria spill out, and active TB begins.

4. Lung tissue damage causes chronic cough, coughing up blood (hemoptysis), weight loss, night sweats, fever — Multiplying bacteria destroy alveoli (air sacs), trigger inflammation, and form cavities (hollow pockets where lung tissue has died). The lungs produce infected mucus and the body coughs for more than three weeks. Blood vessels break, so blood mixes with coughed-up mucus (sputum) (hemoptysis). The immune system runs hot, causing fever and night sweats. Fighting the infection burns calories, causing weight loss.
5. Bacteria spread through bloodstream and lymphatics to distant organs — Infected macrophages travel through lymph vessels and blood vessels, carrying bacteria to lymph nodes (scrofula—painless neck swelling), the meninges (TB meningitis—headache, stiff neck, confusion), the spine (Pott disease—back pain, spinal collapse), the kidneys, the stomach lining, the heart lining (pericarditis), and throughout the lungs (miliary TB—countless tiny nodules, looking like millet seeds on chest X-ray).
6. Cavitory disease risks massive coughing up blood (hemoptysis) — Large cavities erode into pulmonary arteries, causing sudden, life-threatening bleeding (coughing up more than 200 mL of blood at once). This is a medical emergency.
7. Miliary TB and meningitis are the final crash points — Miliary TB (bloodstream spread seeding every organ) causes respiratory failure and multi-organ failure. TB meningitis (bacteria invading the brain's protective layers) causes seizures, stroke, coma, and death if not treated immediately with four-drug therapy and steroids.
8. Every finding traces back to the same upstream break — Chronic cough, coughing up blood (hemoptysis), weight loss, night sweats, fever, cavities, lymph node swelling, meningitis, spine collapse, and miliary spread all follow logically from one failure: macrophages cannot kill *M. tuberculosis*, so the bacteria multiply, damage tissue, and spread wherever macrophages and blood travel.

Symptoms · what the patient feels, and why

- Cough that lasts three weeks or longer: The TB bacteria (*Mycobacterium tuberculosis*) settle in the lungs and trigger swelling (inflammation) and tissue damage. Your body tries to cough out the mucus and debris, but the infection keeps feeding the cycle, so the cough lingers for weeks.
- Coughing up blood or rust-colored coughed-up mucus (sputum) (hemoptysis): The TB infection eats into lung tissue and small blood vessels, letting blood leak into the airways. You then cough up coughed-up mucus (sputum) tinged pink, red, or rust-brown.
- Fever, often with chills: Your immune system releases chemical messengers called cytokines (like interleukin-1 and tumor tissue death (necrosis) factor) that reset the brain's thermostat (the hypothalamus) higher, raising your body temperature to fight the bacteria.

- **Drenching night sweats:** The fever breaks overnight as your body tries to cool down. Hormones (like norepinephrine) signal sweat glands to open wide, soaking your sheets—this is the body's way of dumping extra heat.
- **Unintentional weight loss and loss of appetite:** Cytokines (especially tumor tissue death (necrosis) factor-alpha, once called 'cachectin') ramp up metabolism and suppress hunger signals in the hypothalamus. Meanwhile the infection burns extra calories, so you lose weight even without trying.
- **Fatigue and general weakness:** Fighting a chronic infection drains energy: cytokines tell muscles to break down protein for fuel, and chronic inflammation keeps your body in overdrive, leaving you exhausted.
- **Chest pain, especially with deep breathing or coughing:** TB can inflame the pleura (the thin layers wrapping the lungs). When you breathe deeply, the inflamed layers rub together, triggering sharp pain.
- **Cavities (holes) visible on chest X-ray:** The immune system walls off clumps of bacteria with white blood cells, forming lumps called granulomas. If the center dies and liquefies, it drains out through the airways, leaving a hollow cavity in the lung—a classic TB signature.
- **In children: miliary TB (spread throughout the body) or tuberculous meningitis (infection of the brain's protective lining):** Young children's immune systems are still learning, so TB bacteria can escape the lungs and travel through the bloodstream, seeding tiny nodules (like millet grains—hence 'miliary') in many organs or crossing into the meninges (the membranes around the brain and spinal cord), causing meningitis.

Focused exam

- **Cough lasting more than 3 weeks, often with blood-streaked or rust-colored spit:** The lung is breaking down because the immune cells (macrophages) trapped the bacteria but cannot kill them — the body tries to cough out the infection instead. Blood means the lung tissue itself is damaged.
- **Crackles (wet popping sounds) heard at the top of the lungs, or cavities (holes) seen on chest X-ray:** Tuberculosis bacteria love the upper parts of the lungs because oxygen is highest there — they thrive in oxygen-rich air. Cavities mean the lung tissue has died and left a hole.
- **Night sweats that soak the sheets, weight loss without trying, and fever in the afternoon or evening:** The body is burning massive energy trying to fight the bacteria — the immune system runs hot all the time, draining calories and raising temperature. This is the immune overdrive signal.

- Swollen, firm lymph nodes in the neck (scrofula) or enlarged nodes in the chest on imaging: Tuberculosis can escape the lung and hide in lymph nodes — the body walls off the bacteria with scar tissue but cannot kill them. This means the infection may be spreading beyond the lung.
- Recent close contact (household, shelter, prison, nursing home) with someone who has active tuberculosis: Tuberculosis spreads through the air when an infected person coughs — knowing the source tells you this is a real exposure and others nearby may also be infected and need testing.
- Stiff neck, severe headache, confusion, or trouble staying awake (if the brain lining is involved): Tuberculosis can spread through the blood to the meninges (the lining around the brain and spinal cord) — this is tuberculous meningitis, a life-threatening emergency that needs treatment within hours.

Diagnostics · every test answers a question

- Coughed-up mucus (Sputum) acid-fast bacilli (AFB) smear — 3 separate morning samples → Are tuberculosis bacteria visible right now in the spit under the microscope?
- Coughed-up mucus (Sputum) mycobacterial culture (solid or liquid media) → Can we grow the bacteria in the lab to confirm it is *M. tuberculosis* and test which drugs kill it?
- Nucleic acid amplification test (NAAT), such as GeneXpert MTB/RIF → Can we detect tuberculosis DNA in the coughed-up mucus (sputum) within hours, and is the bacteria resistant to rifampin?
- Chest X-ray (posteroanterior and lateral views) → Where in the lungs is the damage, and how bad is it?
- Tuberculin skin test (TST, Mantoux test) or interferon-gamma release assay (IGRA, such as QuantiFERON) → Has the immune system ever seen tuberculosis bacteria before?
- HIV test (fourth-generation antigen/antibody or RNA if acute infection suspected) → Is the immune system weakened by HIV, which makes tuberculosis much more dangerous?
- Complete blood count (CBC) with differential → Is the body making extra white blood cells to fight infection, or is the bone marrow being hurt by the disease?
- Red blood cell (Erythrocyte) sedimentation rate (ESR) or C-reactive protein (CRP) → How much inflammation is the body fighting right now?

Treatment logic

- RIPE regimen: rifampin, isoniazid, pyrazinamide, ethambutol — all four drugs daily for the first 2 months (intensive phase) → These four drugs work together to kill *M. tuberculosis* hiding inside macrophages and in oxygen-poor pockets of the lung. Rifampin stops the bacteria from copying their DNA. Isoniazid punches holes in the bacterial cell wall. Pyrazinamide works in acidic, low-oxygen areas where the bacteria sleep. Ethambutol blocks the bacteria from building their protective waxy coat. Using all four at once kills the bacteria fast and stops them from becoming resistant.
- Continuation phase: rifampin plus isoniazid daily (or 3 times per week) for 4 more months after the first 2 months → Kills the remaining slow-growing bacteria hiding in cavities, scar tissue, and low-oxygen corners of the lung where they multiply very slowly. This extended phase prevents relapse — without it, the bacteria wake up and the disease comes back.
- Pyridoxine (vitamin B6) 25–50 mg daily, given with isoniazid → Prevents peripheral neuropathy (nerve damage causing numbness, tingling, and burning pain in hands and feet) caused by isoniazid, which depletes vitamin B6. Pyridoxine replaces what isoniazid uses up.
- Airborne isolation (negative-pressure room, N95 respirators for staff) until coughed-up mucus (sputum) AFB smears are negative on 3 consecutive samples (usually after 2 weeks of treatment) → Stops the patient from breathing tuberculosis bacteria into the air where nurses, family, roommates, and other patients can breathe them in. This breaks the transmission chain and protects others.
- Directly observed therapy (DOT): a healthcare worker or trained observer watches the patient swallow every dose → Ensures the patient actually takes the medicine every single day for the full 6 months — missing doses lets bacteria survive and become drug-resistant. DOT prevents treatment failure and stops the creation of multidrug-resistant tuberculosis (MDR-TB).
- Latent tuberculosis infection (LTBI) treatment: isoniazid daily for 6–9 months, OR rifampin daily for 4 months, OR isoniazid + rifapentine weekly for 3 months (3HP regimen) — for people with positive TST/IGRA but no active disease → Kills dormant (sleeping) tuberculosis bacteria before they wake up and cause active lung disease. Reduces the risk of reactivation from ~10% lifetime to <1%. Protects the person and stops future transmission.
- Drug-resistant TB regimen (for rifampin-resistant or multidrug-resistant TB): bedaquiline, linezolid, fluoroquinolone (levofloxacin or moxifloxacin), plus 1–2 additional agents for 18–20 months → Kills tuberculosis bacteria that survived standard drugs because they have mutations in their DNA that block rifampin or isoniazid from working. Longer treatment and stronger drugs are needed to cure drug-resistant strains.

Medications

Isoniazid (INH) · First-line anti-tuberculosis antibiotic

Isoniazid stops TB bacteria from building their protective outer wall. TB bacteria have a thick, waxy coat (called a mycolic acid layer) that acts like armor and lets them hide inside immune cells. Isoniazid blocks the enzyme (a tiny protein machine called InhA) that assembles this waxy armor. Without the armor, the bacteria can't grow or survive, and the body's immune cells can finally kill them.

1. TB bacteria are swallowed by macrophages but survive inside them because of their thick waxy wall.
2. Isoniazid enters the macrophage and the TB bacteria.
3. Inside the bacteria, isoniazid is activated by an enzyme called KatG (a bacterial protein).
4. Activated isoniazid blocks InhA, the enzyme that makes mycolic acid (the waxy armor).
5. Without mycolic acid, the bacteria's wall becomes fragile and leaks.
6. The bacteria can no longer grow, divide, or protect themselves.
7. The immune system and other drugs can now kill the weakened bacteria.

SAFETY WATCH

Hepatotoxicity (liver damage): Isoniazid can raise liver enzymes (AST, ALT). Check liver tests before starting and monthly if the patient has liver disease, drinks alcohol regularly, is over 35, is pregnant, or has HIV. Stop the drug if liver enzymes rise more than five times normal or if the patient has symptoms like yellow skin (jaundice), nausea, or belly pain. · Peripheral neuropathy (nerve damage in hands and feet): Isoniazid lowers vitamin B6 (pyridoxine) in the body, which nerves need to stay healthy. This causes tingling, numbness, or burning in the fingers and toes. ALWAYS give pyridoxine 25–50 mg daily with isoniazid to prevent this, especially in people with diabetes, HIV, alcohol use, malnutrition, or pregnancy. · Drug interactions: Isoniazid slows the liver's breakdown of many drugs (it inhibits cytochrome P450 enzymes), so levels of phenytoin, warfarin, and some antifungals can rise and cause side effects. Monitor and adjust doses as needed. · Rare reactions: Rarely causes a lupus-like syndrome (joint pain, rash, fever) or seizures in overdose.

Rifampin (RIF) · First-line anti-tuberculosis antibiotic (rifamycin class)

Rifampin stops TB bacteria from copying their DNA instructions into RNA, which is the step they need to make new proteins and grow. It does this by jamming the bacteria's RNA polymerase (the machine that reads DNA and writes RNA). Without RNA, the bacteria can't make the proteins they need to survive. Rifampin is one of the few drugs that can kill both

actively growing TB bacteria and slow-growing or dormant bacteria hiding in tissues, which is why it shortens treatment from 12–18 months down to 6 months.

1. Rifampin enters TB bacteria.
2. It binds tightly to the bacteria's RNA polymerase enzyme.
3. RNA polymerase can no longer read the bacteria's DNA or make RNA.
4. Without RNA, the bacteria can't make essential proteins.
5. The bacteria stop growing and die, even if they were dormant.
6. Rifampin also boosts the killing power of other TB drugs by making the bacteria's wall more permeable.

SAFETY WATCH

Drug interactions (extremely important): Rifampin is a powerful inducer of liver enzymes (CYP3A4, CYP2C9, CYP2C19). It speeds up the breakdown of dozens of drugs, lowering their levels and effectiveness. This includes: antiretrovirals (HIV drugs—use rifabutin instead or adjust doses carefully), hormonal birth control (use non-hormonal methods), warfarin, methadone, antifungals, some diabetes drugs, tacrolimus, cyclosporine, and many others. Always check for interactions before starting rifampin. · Hepatotoxicity (liver damage): Rifampin can raise liver enzymes, especially when combined with isoniazid and pyrazinamide. Monitor liver tests as for isoniazid. · Orange discoloration: Rifampin turns urine, tears, sweat, and saliva bright orange-red. This is harmless but can permanently stain soft contact lenses. Warn patients so they are not alarmed. · Flu-like syndrome: If rifampin is taken inconsistently (less than twice weekly), it can cause sudden fever, chills, muscle aches, and low platelets (thrombocytopenia) or kidney problems. Directly observed therapy helps prevent this. · Rare reactions: Rarely causes severe allergic reactions, low platelets, or kidney injury.

Pyrazinamide (PZA) · First-line anti-tuberculosis antibiotic

Pyrazinamide is unique because it works best in acidic, low-oxygen environments—exactly the conditions inside macrophages and in the center of granulomas (the walled-off clumps of immune cells and bacteria in the lungs). In these acidic pockets, pyrazinamide is converted by a bacterial enzyme (pyrazinamidase) into pyrazinoic acid, which disrupts the bacteria's energy production and membrane transport. This kills slow-growing, semi-dormant TB bacteria that other drugs miss. Pyrazinamide shortens treatment by clearing these hidden bacteria early, which is why it is used only in the first 2 months of therapy.

1. TB bacteria hide inside macrophages and granulomas, where the environment is acidic and low in oxygen.
2. Pyrazinamide enters these bacteria.

3. A bacterial enzyme (pyrazinamidase) converts pyrazinamide into pyrazinoic acid.
4. Pyrazinoic acid lowers the pH even more inside the bacteria and disrupts their membrane function and energy production.
5. The bacteria can no longer maintain their internal balance or make energy.
6. Slow-growing, semi-dormant bacteria die.
7. This clears the bacteria hiding in hard-to-reach spots, preventing relapse.

SAFETY WATCH

Hepatotoxicity (liver damage): Pyrazinamide is the most liver-toxic of the first-line TB drugs. It can cause serious hepatitis, especially in the first 2 months. Monitor liver enzymes (AST, ALT) before starting and monthly. Stop the drug if enzymes rise more than five times normal or if the patient has yellowing of the skin and eyes (jaundice), nausea, or belly pain. · Hyperuricemia and gout: Pyrazinamide raises uric acid levels in the blood by blocking the kidneys from getting rid of it. This can cause gout (sudden, severe joint pain and swelling, usually in the big toe). Check uric acid levels if the patient has joint pain. Treat gout attacks with NSAIDs or colchicine, but do NOT stop pyrazinamide unless gout is severe or recurrent. Do not routinely give allopurinol to prevent gout—it is not recommended. · GI upset: Nausea and loss of appetite are common but usually mild. · Joint pain (Arthralgia) (joint pain): Mild joint aches are common and usually do not require stopping the drug.

Ethambutol (EMB) · First-line anti-tuberculosis antibiotic

Ethambutol blocks the bacteria's ability to build arabinogalactan, a key sugar-based scaffold in the TB bacteria's cell wall. It does this by inhibiting arabinosyl transferases (enzymes that assemble this scaffold). Without arabinogalactan, the bacteria's thick waxy wall becomes incomplete and weak, and the bacteria can't grow or survive. Ethambutol is included in the first 2 months of treatment mainly to protect against drug resistance—if the TB bacteria turn out to be resistant to isoniazid (which isn't known until culture results come back after several weeks), ethambutol helps keep the other drugs working.

1. Ethambutol enters TB bacteria.
2. It blocks arabinosyl transferase enzymes, which build arabinogalactan (a sugar scaffold in the cell wall).
3. Without arabinogalactan, the bacteria can't finish building their protective waxy wall.
4. The bacteria's wall becomes fragile and leaks.
5. The bacteria stop growing and become more vulnerable to immune attack and other drugs.
6. Ethambutol also prevents resistant mutants from taking over if one of the other drugs fails.

SAFETY WATCH

Optic neuritis (eye nerve damage): Ethambutol can damage the optic nerve, causing loss of color vision (especially red-green), blurry vision, or blind spots. This is dose-related and more common at doses above 15–25 mg/kg/day or in patients with kidney problems (ethambutol is cleared by the kidneys, so it builds up if kidneys are weak). Check vision and color perception before starting and monthly during treatment. Ask patients to report any vision changes immediately. Stop ethambutol right away if vision problems occur—damage may be reversible if caught early but can be permanent if the drug is continued. · Dose adjustment in kidney disease: Lower the dose or increase the dosing interval if the patient's estimated glomerular filtration rate (eGFR) is below 30 mL/min. · Avoid in young children when possible: Ethambutol is harder to use in children under 5 years old because they cannot reliably report vision changes. Use it only if drug resistance is suspected and monitor closely. · Rare reactions: Rarely causes peripheral neuropathy (nerve damage in hands and feet), rash, or elevated uric acid.

Pyridoxine (Vitamin B6) · Vitamin supplement (neuropathy prevention)

Pyridoxine is vitamin B6, which nerves need to stay healthy and function properly. Isoniazid lowers vitamin B6 levels in the body by interfering with its metabolism. Without enough B6, nerves can't make the proteins and neurotransmitters they need, and they become damaged, causing tingling, numbness, or burning pain in the hands and feet (peripheral neuropathy). Giving pyridoxine alongside isoniazid prevents this nerve damage by keeping B6 levels normal.

1. Isoniazid is taken for TB treatment.
2. Isoniazid lowers vitamin B6 (pyridoxine) levels in the body.
3. Nerves need B6 to make myelin (the insulation around nerves) and neurotransmitters (chemical messengers).
4. Without enough B6, nerves become damaged and send abnormal signals.
5. This causes tingling, numbness, burning, or pain in the fingers and toes.
6. Taking pyridoxine 25–50 mg daily keeps B6 levels normal.
7. Nerves stay healthy and neuropathy is prevented.

SAFETY WATCH

Very safe: Pyridoxine at the doses used for TB (25–50 mg daily) is extremely safe and has almost no side effects. · High doses (above 200 mg/day for months) can rarely cause sensory neuropathy (nerve damage), but this does not happen at the low prevention doses used with isoniazid.

Rifapentine (used with isoniazid in the 3HP regimen for latent TB) · Rifamycin antibiotic (long-acting)

Rifapentine works the same way as rifampin—it jams the TB bacteria's RNA polymerase enzyme so the bacteria can't make RNA or proteins—but it stays in the body much longer (has a longer half-life). This allows it to be given once a week instead of daily. In the 3HP regimen for latent TB infection (infection without active disease), rifapentine is combined with isoniazid and given once weekly for 12 weeks. This is much shorter and more convenient than 6–9 months of daily isoniazid, and people are more likely to complete it. Rifapentine kills dormant TB bacteria hiding in the body before they can wake up and cause active TB disease.

1. Dormant TB bacteria are hiding in the body after infection but have not caused disease yet.
2. Rifapentine enters these bacteria.
3. It binds to and blocks RNA polymerase.
4. The bacteria can't make RNA or proteins.
5. The bacteria die, preventing future active TB disease.
6. Because rifapentine lasts a long time in the body, once-weekly dosing keeps drug levels high enough to kill bacteria all week.

SAFETY WATCH

Drug interactions: Like rifampin, rifapentine strongly induces liver enzymes (CYP3A4 and others), so it lowers levels of many drugs including antiretrovirals (HIV drugs), hormonal birth control, warfarin, and others. Check for interactions before starting. Use non-hormonal birth control during treatment. · Flu-like reactions: Rifapentine can cause sudden fever, chills, muscle aches, dizziness, or low blood pressure, especially if doses are missed and then restarted. This is more common with once-weekly dosing. Warn patients and consider stopping if reactions are severe. · Hepatotoxicity (liver damage): Can raise liver enzymes, especially when combined with isoniazid. Monitor liver tests before starting and if the patient has symptoms. · Hypersensitivity: Rarely causes rash, low platelets, or severe allergic reactions. · Orange discoloration: Like rifampin, turns body fluids orange-red. Warn patients. · Not for use in HIV patients on certain antiretrovirals: Rifapentine interacts severely with many HIV drugs. Use daily rifampin-based regimens instead, or consult an infectious disease specialist.

Bedaquiline (for multidrug-resistant TB, MDR-TB) · ATP synthase inhibitor (newer TB antibiotic)

Bedaquiline blocks the bacteria's ATP synthase, the enzyme that makes ATP (the energy currency of cells). TB bacteria need ATP to survive, grow, and maintain their thick protective wall. By shutting down ATP production, bedaquiline starves the bacteria of energy, causing

them to die. Bedaquiline is one of the few drugs that works against multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), strains that do not respond to isoniazid and rifampin. It is always used in combination with other second-line TB drugs, never alone.

1. Multidrug-resistant TB bacteria survive because they have mutations that block isoniazid and rifampin.
2. Bedaquiline enters these bacteria.
3. It binds to ATP synthase, the enzyme that makes ATP (energy).
4. ATP synthase is blocked and stops making ATP.
5. Without ATP, the bacteria can't power essential processes like building their cell wall or pumping out toxins.
6. The bacteria run out of energy and die, even if they are resistant to other drugs.

SAFETY WATCH

QT prolongation (heart rhythm problem): Bedaquiline can lengthen the QT interval on an ECG, which raises the risk of a dangerous heart rhythm called torsades de pointes. Get a baseline ECG before starting, and repeat ECGs at 2, 12, and 24 weeks. Avoid bedaquiline or monitor very closely if the patient has a long QT already, low potassium or magnesium, or is taking other QT-prolonging drugs (like fluoroquinolones, which are also used for MDR-TB). · Hepatotoxicity (liver damage): Can raise liver enzymes. Monitor liver tests monthly. · Drug interactions: Bedaquiline is broken down by liver enzyme CYP3A4. Rifampin and rifapentine speed up CYP3A4 and lower bedaquiline levels (so avoid using them together). Some HIV drugs (efavirenz, nevirapine, lopinavir/ritonavir) also interact; specialist guidance is needed. · Nausea and joint pain: Common but usually manageable. · Mortality signal: Early studies showed a small increase in deaths in the bedaquiline group, but the reasons were unclear and the benefit in curing MDR-TB is considered to outweigh this risk. Use only when needed and under specialist supervision.

Pretomanid (for highly resistant TB, used with bedaquiline and linezolid in the BPAL regimen) · Nitroimidazole antibiotic (newer TB drug)

Pretomanid is activated inside TB bacteria and creates toxic nitrogen radicals (reactive molecules) that damage the bacteria's DNA, cell wall, and proteins. It works against both actively growing bacteria and dormant bacteria hiding in low-oxygen environments (like the center of granulomas). Pretomanid is used in the BPAL regimen (bedaquiline, pretomanid, linezolid) for extensively drug-resistant TB (XDR-TB) or treatment-intolerant MDR-TB. This is a 6-month, all-oral regimen that replaced much longer, more toxic injectable regimens. Pretomanid must be used with bedaquiline and linezolid—never alone.

1. Highly resistant TB bacteria survive because standard drugs don't work.

2. Pretomanid enters the bacteria.
3. A bacterial enzyme activates pretomanid, creating toxic nitrogen radicals.
4. These radicals attack the bacteria's DNA, cell wall, and proteins.
5. The bacteria's machinery breaks down and the bacteria die.
6. Pretomanid also disrupts mycolic acid synthesis (cell wall building), adding another way to kill bacteria.
7. It works even on slow-growing, dormant bacteria in oxygen-poor spots.

SAFETY WATCH

Hepatotoxicity (liver damage): Pretomanid can raise liver enzymes and rarely cause serious liver injury. Monitor liver tests before starting and every 2 weeks for the first 2 months, then monthly. Stop if liver enzymes rise more than five times normal or if yellowing of the skin and eyes (jaundice) or symptoms appear. · QT prolongation: Can lengthen the QT interval (like bedaquiline, which is given with it). Get baseline and follow-up ECGs. Correct low potassium and magnesium. · Peripheral neuropathy (nerve damage): Linezolid (given with pretomanid) commonly causes neuropathy; pretomanid itself is less likely to, but the combination raises the risk. Monitor for tingling, numbness, or burning in hands and feet. · Myelosuppression (low blood counts): The BPaL regimen (especially linezolid) can lower red blood cells, white blood cells, and platelets. Monitor complete blood counts regularly. · Avoid alcohol: Pretomanid may cause a disulfiram-like reaction (flushing, nausea, vomiting) if alcohol is consumed. · Drug interactions: Pretomanid is metabolized by liver enzymes. Strong enzyme inducers (like rifampin) lower pretomanid levels. Use only under specialist guidance.

Linezolid (for multidrug-resistant TB, part of BPaL and other MDR-TB regimens) · Oxazolidinone antibiotic

Linezolid stops TB bacteria from making new proteins by blocking the ribosome (the bacteria's protein-making machine) at an early step. It binds to the 50S subunit of the bacterial ribosome and prevents the formation of the initiation complex, so protein synthesis never gets started. Without proteins, the bacteria can't grow, repair themselves, or survive. Linezolid works against multidrug-resistant and extensively drug-resistant TB and is a key part of the BPaL regimen (with bedaquiline and pretomanid) and other MDR-TB regimens.

1. Multidrug-resistant TB bacteria resist standard drugs.
2. Linezolid enters the bacteria.
3. It binds to the 50S ribosome subunit.
4. The ribosome can't start making proteins.
5. Without proteins, the bacteria can't build enzymes, repair cell walls, or grow.

6. The bacteria stop multiplying and die.

SAFETY WATCH

Myelosuppression (low blood counts): Linezolid commonly lowers red blood cells (anemia), white blood cells (raising infection risk), and platelets (raising bleeding risk), especially after weeks to months of use. Monitor complete blood counts every 2 weeks. If counts drop severely, reduce the dose (e.g., from 600 mg daily to 300 mg daily or three times weekly) or stop linezolid. · Peripheral neuropathy (nerve damage): Linezolid often causes tingling, numbness, burning, or pain in the hands and feet, especially with prolonged use (over 2–3 months). This can be permanent. Monitor symptoms monthly. If neuropathy develops, reduce the dose or stop linezolid if possible. · Optic neuropathy (eye nerve damage): Linezolid can damage the optic nerve, causing blurry vision or loss of color vision. Check vision before starting and monthly. Stop linezolid if vision changes occur. · Lactic acidosis (acid from oxygen-starved tissues): Linezolid can damage mitochondria (the cell's energy factories), causing a buildup of lactic acid in the blood. This is rare but can be life-threatening. Symptoms include nausea, vomiting, fast breathing, confusion, or muscle pain. Stop linezolid if lactic acidosis is suspected. · Serotonin syndrome: Linezolid weakly inhibits monoamine oxidase (MAO), so combining it with serotonergic drugs (SSRIs, SNRIs, tramadol, meperidine, dextromethorphan) can cause serotonin syndrome (agitation, confusion, fast heart rate, high blood pressure, muscle rigidity, fever). Avoid these combinations or monitor very closely. · Avoid tyramine-rich foods: Because linezolid inhibits MAO, eating tyramine-rich foods (aged cheese, cured meats, soy sauce, draft beer) can cause dangerously high blood pressure. Counsel patients to avoid these foods. · GI upset: Nausea and diarrhea are common but usually mild.

Red flags

- Coughing up blood (hemoptysis)
- Severe trouble breathing or shortness of breath at rest
- Confusion, stiff neck, or severe headache (signs of meningitis)
- Rapid weight loss (more than 10% of body weight in weeks)
- Known contact with someone who has active TB and new symptoms

Nursing priorities

1. Place patient in airborne isolation room (negative pressure room with door closed) and wear N95 respirator mask before entering — TB bacteria travel through tiny airborne droplets (droplet nuclei) that stay floating in air for hours. Standard surgical masks do not filter particles this small. Negative pressure keeps contaminated air from escaping the room. This protects staff, other patients, and visitors from infection.
2. Collect three coughed-up mucus (sputum) samples (morning is best) for acid-fast bacilli smear and culture before first antibiotic dose — Coughed-up mucus (Sputum) (mucus coughed from deep lungs) testing confirms diagnosis and identifies drug resistance. The acid-fast stain shows TB bacteria within hours. Culture grows bacteria to test which medicines work, but takes 6 to 8 weeks. Starting treatment before collection makes test results falsely negative.
3. Administer all four RIPE medicines (rifampin, isoniazid, pyrazinamide, ethambutol) together at the same time each day, and watch the patient swallow every pill — Directly observed therapy (DOT) prevents patients from skipping doses or stopping early, which creates drug-resistant bacteria. Taking all four drugs together kills bacteria faster and stops resistance from developing. Consistency in timing keeps blood levels steady for best killing power.
4. Give pyridoxine (vitamin B6) 25 to 50 mg by mouth daily with the isoniazid dose — Isoniazid blocks the body from using vitamin B6. Low B6 causes peripheral neuropathy (nerve damage in hands and feet with tingling, numbness, and pain). Pyridoxine prevents this side effect. Diabetics, alcoholics, malnourished patients, and pregnant women need this supplement most.
5. Check baseline liver function tests (ALT, AST, bilirubin) and teach patient to report yellowing eyes, dark urine, nausea, or right upper belly pain immediately — Rifampin, isoniazid, and pyrazinamide all can cause hepatotoxicity (liver damage). The liver breaks down these drugs, and combining them increases risk. Liver enzymes (ALT and AST) rising 3 to 5 times normal means stop medicines immediately. Yellowing of the skin and eyes (Jaundice) (yellow skin) is a late, dangerous sign.
6. Test vision and red-green color discrimination before starting ethambutol, then monthly during treatment — Ethambutol causes optic neuritis (inflammation of the eye nerve), leading to blurry vision, blind spots, and loss of red-green color vision. Damage can be permanent if not caught early. Patients must report vision changes immediately so the drug can be stopped.

7. Educate patient that urine, sweat, and tears will turn orange-red from rifampin, and soft contact lenses will stain permanently — Rifampin is excreted (removed from body) in all body fluids and colors them bright orange. Patients panic thinking they have blood in urine or are bleeding from eyes. Knowing this is harmless and temporary improves adherence (willingness to keep taking medicine). Warn about ruined contacts before starting treatment.
8. Continue airborne isolation until patient has three negative coughed-up mucus (sputum) smears on different days after starting treatment — Living bacteria in coughed-up mucus (sputum) mean the patient is contagious. Treatment kills bacteria within 2 weeks usually, but confirmation requires negative smears. Cough may continue for months even when not contagious. Three negative tests ensure the patient cannot spread infection before ending isolation.

Sources

- WHO Global Tuberculosis Report 2024
- ATS/CDC/IDSA Clinical Practice Guidelines for Treatment of Drug-Susceptible Tuberculosis 2016
- CDC Tuberculosis Guidelines 2023
- Cochrane Reviews on Tuberculosis Diagnosis and Treatment

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