Tuberculosis

Isolate first · Then decide active or latent, and which regimen

ISOLATE ON SUSPICION
not on confirmation

SUSPECT AND ISOLATE *the decision that protects everyone else*

THE PICTURE

Cough > 2–3 weeks, fever, **drenching night sweats**, weight loss, hemoptysis. **Risk factors:** birth or travel in an endemic country, HIV, homelessness, incarceration, close contact, **TNF inhibitors** or other immunosuppression, silicosis, diabetes, malnutrition.

ISOLATE IMMEDIATELY

Negative-pressure airborne isolation room with N95 respirators for anyone with suspected pulmonary TB — **before** any test returns. Waiting for confirmation exposes staff and other patients for days.

IMAGING

Upper lobe cavitation in reactivation disease; **miliary** pattern in disseminated disease. In HIV with low CD4 the film can be **atypical or normal**, so a clear chest X-ray does not exclude TB in the immunosuppressed.

CONFIRM IT *three sputa, a molecular test, and a culture*

Test	What it gives you
Sputum AFB smear × 3	Collected on separate occasions, at least 8 hours apart with one early morning. **Smear indicates infectiousness** but is insensitive — a negative smear does not exclude TB.
Nucleic acid amplification (NAAT)	Rapid confirmation of **M. tuberculosis complex** and detection of **rifampin resistance** within hours. Should be done on at least one specimen in every suspected case.
Mycobacterial culture	**The gold standard** and the only way to get full **drug susceptibility testing**. Takes weeks — but it is what ultimately determines the regimen, so always send it.
IGRA or tuberculin skin test	**For latent infection only.** They cannot distinguish latent from active disease and **must not be used to rule out active TB** — both can be negative in severe or disseminated disease.
Extrapulmonary	Send tissue or fluid for AFB, culture and histology. **Pleural, pericardial and CSF fluid have low yield** — adenosine deaminase helps in pleural and peritoneal disease, and biopsy substantially improves the diagnostic rate.

TREAT ACTIVE DISEASE *two regimens now, and the shorter one is genuinely new*

1. **Standard 6-month regimen: RIPE** — rifampin, isoniazid, pyrazinamide and ethambutol — for **2 months**, then **rifampin and isoniazid for 4 months**. Ethambutol can be dropped once susceptibility confirms a fully sensitive organism.
2. **4-month rifapentine-moxifloxacin regimen: isoniazid, rifapentine, pyrazinamide and moxifloxacin for 2 months**, then **isoniazid, rifapentine and moxifloxacin** for the continuation phase — **17 weeks in total**. Shown as effective as the 6-month regimen.
3. **Who qualifies for the short regimen:** aged **≥ 12 years**, **drug-susceptible pulmonary TB** not known or suspected to be resistant, and no contraindication. **People with HIV are eligible if CD4 is ≥ 100** and they are on an antiretroviral regimen without drug interactions with rifapentine.
4. **Add pyridoxine (vitamin B6)** with isoniazid to prevent peripheral neuropathy — especially in pregnancy, diabetes, alcohol use, malnutrition, HIV and renal failure.
5. **Use directly observed therapy** where possible, and **notify public health immediately**. Contact tracing and adherence support are part of the treatment, not an administrative afterthought.

DRUG TOXICITY & LATENT INFECTION *what to warn about, and what to give*

MONITOR FOR

Hepatotoxicity — isoniazid, rifampin and pyrazinamide all cause it; check baseline and serial LFTs and warn about symptoms. **Rifampin**: orange secretions, and a **potent CYP inducer** that wrecks levels of ART, warfarin, contraceptives and many others. **Ethambutol**: optic neuritis — baseline and periodic **visual acuity and color vision**. **Pyrazinamide**: hyperuricemia and arthralgia.

LATENT TB

Always exclude active disease first — treating latent TB with a single drug when disease is active generates resistance. Preferred short regimens: **3HP** (isoniazid plus rifapentine weekly for 12 weeks), **4R** (rifampin daily for 4 months), or **3HR**. Longer isoniazid monotherapy is now a second-line option. **Screen before starting TNF inhibitors** or other biologics.

SPECIAL SITUATIONS *where the standard regimen changes*

Situation	What changes
HIV co-infection	**Start TB treatment first**, then ART — within **2 weeks if CD4 is low**, otherwise by 8 weeks. Expect **paradoxical IRIS**. **Rifampin interacts severely with antiretrovirals**; rifabutin is often substituted. **Exception: TB meningitis**, where early ART increases harm and initiation is deferred.
Pregnancy	**Treat — untreated TB is far more dangerous than the drugs.** Rifampin, isoniazid and ethambutol are used; **give pyridoxine**. **Streptomycin is contraindicated** (fetal ototoxicity). Add vitamin K around delivery with rifampin.
CNS or pericardial disease	**Add corticosteroids** — they reduce mortality in TB meningitis and constriction in pericardial disease. **Extend therapy**, typically to 9–12 months for CNS involvement.
Drug resistance	**Rifampin resistance on NAAT is a red flag** requiring immediate expert referral. MDR-TB needs a **multi-drug regimen including bedaquiline**, managed by a specialist service, never assembled ad hoc.
Renal or hepatic impairment	**Ethambutol and pyrazinamide need renal dose adjustment**; rifampin and isoniazid are largely hepatically cleared. In significant liver disease, involve specialists before starting a three-hepatotoxin regimen.

PEARLS & PITFALLS

- **Isolate on suspicion, not on confirmation.** The commonest institutional failure is a delayed isolation order while awaiting smears.
- **A negative IGRA or skin test does not exclude active TB** and should never be used for that purpose.
- **Always send culture**, even when the NAAT is positive — only culture gives full susceptibility, and resistance changes everything.
- **Never add a single drug to a failing regimen** — it is the classic route to amplified resistance.
- **Check the rifampin interactions** before discharge, particularly with antiretrovirals, anticoagulants and contraception.
- **Exclude active disease before treating latent infection**, and give pyridoxine with isoniazid every time.

References: CDC Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the Treatment of Drug-Susceptible Pulmonary Tuberculosis, United States (MMWR, 2022) · Study 31/A5349 (NEJM, 2021) · ATS/CDC/IDSA treatment guidelines for drug-susceptible tuberculosis.

roundsrx.com
roundsrx Infographic Series · #103