

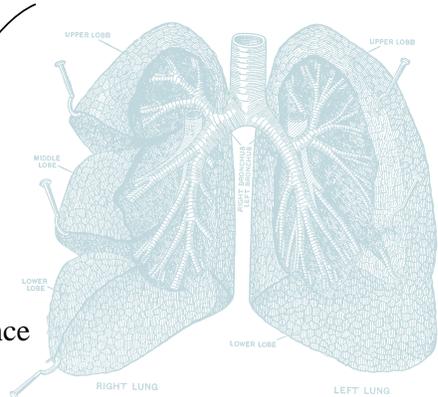
THE NEW YORK CITY DEPARTMENT OF HEALTH

Tuberculosis Treatment

Because of renewed tuberculosis (TB) control efforts in New York City, there has been a dramatic decrease since 1992 in the number of cases of tuberculosis, especially multidrug-resistant TB (MDRTB). To ensure that tuberculosis *remains* under control, the need for vigilance is crucial. Almost all cases of TB can be effectively treated, and treatment is the key to breaking the chain of disease transmission. **Therefore, the top priority remains to cure patients with active TB.** | Prompt diagnosis (**think TB!**), appropriate initial treatment (**begin all previously untreated patients on at least 4 anti-TB drugs**), and the use of **directly observed therapy (DOT)** all improve the chance of cure. | As part of clinical care:

- Every initial isolate of *Mycobacterium tuberculosis* should be submitted for drug-susceptibility testing.
- Sputum samples should be obtained at least monthly until culture conversion to negative can be documented. In addition, a sputum sample should be obtained at the end of treatment to document cure.
- Special attention should be given to individuals infected with both *M. tuberculosis* and HIV. The introduction of antiretroviral therapy for the treatment of HIV infection, while greatly improving the life of many, has complicated the treatment of TB in HIV-infected persons. Seeking expert advice is key for the optimal management of patients with both diseases.
- A single drug should **NEVER** be added to a failing regimen.

As the incidence of MDRTB declines in



New York City, fewer physicians have had the opportunity to develop and maintain clinical expertise in the management of these complex cases; *treatment of MDRTB should not be attempted without expert consultation.* | The third edition of this report, originally published in 1992, updates physicians on the most recent TB treatment guidelines. A summary of the major changes for this edition appears on page 3. New tables are provided that indicate foreign countries where TB is prevalent, organize the basics of treatment along a timeline, describe doses and toxicities of anti-TB medications, recommend anti-TB regimens for HIV-infected persons, and review available evidence on the management of patients in pregnancy, with TB meningitis, and with renal insufficiency. Recommendations are offered based on the best current consensus of published and clinical data. An updated resource directory appears on page 4. | **Our TB Hotline number for physicians is (212) 788-4162.** Call during business hours to report a case, or for information about your patient's previous TB treatment, including drug-susceptibility results.

Ten Basics

on the Diagnosis, Treatment, and Prevention of Tuberculosis

SCREENING

1 Think TB!

Consider the diagnosis of active tuberculosis in any patient with chronic cough and fever, especially if the person has a risk factor for HIV infection or other immunosuppression. Others at increased risk for TB disease include:

- Close contacts of a person with pulmonary or laryngeal TB disease
- Persons with medical risk factors for TB disease other than HIV infection (e.g., diabetes, leukemia, Hodgkin's disease)
- Persons with radiographic evidence of old, healed TB
- Employees or residents of hospitals, correctional facilities, homeless shelters, or nursing homes
- Foreign-born persons from countries where TB is common (see Table 1)
- Injection drug users
- Persons whose skin tests have converted within the last 2 years

Isolate hospitalized patients as soon as active TB disease is suspected or confirmed. Prompt diagnosis, effective respiratory isolation, appropriate treatment, and realistic plans for treatment completion after hospital discharge are all essential to reducing the risk of nosocomial spread of TB (see References 4 and 9).

2 Report suspected or confirmed cases of active TB to the New York City Department of Health.

Medical providers and infection control practitioners are required by law to report all suspected and confirmed cases of TB to the Department of Health within 24 hours of the time the diagnosis is first suspected. To report a case, call the TB Hotline at (212) 788-4162. (A completed TB Case Report [form TB76] must follow within 48 hours.)

3 Always take a detailed TB treatment history and obtain drug-susceptibility studies on initial TB isolates.

Take a complete history of prior anti-TB treatment. For example, ask the patient if she has ever taken a medicine that turned her urine and tears orange-red (rifampin) or received shots (streptomycin) for weeks or months. In addition, the Department of Health recommends that susceptibility testing be performed on all initial and final isolates of *M. tuberculosis*. The Department of Health maintains a registry of patients with active TB, their treatment histories, and the results of their drug-susceptibility tests. For information, physicians are encouraged to call the TB Hotline at (212) 788-4162.

4 Begin all previously untreated TB patients on at least 4 anti-TB drugs.

Patients with active disease who have never been treated for TB before should be started on isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) (see Tables 2 and 3). Previously treated patients should receive at least 2, and preferably 3 to 5, medications they have not received before and to which their isolate has documented susceptibility, if drug susceptibility results are available. **NEVER ADD A**

SINGLE DRUG TO A FAILING REGIMEN. To do so may promote the development of further drug resistance.

5 Provide ongoing TB care.

Ongoing care is a complex art. It is strongly recommended that TB treatment be undertaken in consultation with a physician experienced in its management. Patients with suspected or confirmed TB and their contacts can be referred to a Department of Health Chest Clinic for consultation or ongoing care. In addition, physicians can obtain expert medical consultation by calling the Department of Health at (212) 442-9968. (Ask for the physician-on-call.)

- Because immune status can be a critical factor in treatment, voluntary, confidential HIV testing and counseling should be offered to patients.
- Patients should be thoroughly evaluated at the first visit and monitored at least monthly (see Table 2). Most patients with isoniazid- and rifampin-susceptible TB need monthly sputum tests only until cultures become negative (documented by 2 negative cultures taken at least 1 month apart). Patients who are not adherent, who show signs of relapse, or who are prescribed a non-rifamycin or isoniazid regimen, require more frequent monitoring. At the end of treatment, a sputum specimen should be examined to document cure.
- If a patient's sputum cultures remain positive after 4 months of treatment, the possibility of malabsorption, patient nonadherence to treatment, or disease due to drug-resistant organisms should be explored.

6 Give top priority to completion of treatment.

If every patient with active TB were promptly identified, appropriately treated, and completed a full anti-TB regimen, the spread of TB would stop. *The time to plan for treatment completion is immediately on diagnosis.* Ideally, every TB patient should receive every dose of anti-TB medication within a program of directly observed therapy (DOT), in which a health-care worker or other person watches the patient take the medicine. Without adequate supervision, many patients abandon treatment before they are cured. When this happens, patients remain ill, they may infect others, and they are at risk for developing multidrug-resistant TB, a potentially deadly form of the disease. DOT can be provided at New York City Department of Health Chest Clinics or by Department of Health outreach workers at a patient's home or workplace, or at other locations. For help arranging DOT for your patients, call the Health Department at (212) 442-9777/78.

7 Never treat multidrug-resistant TB (MDRTB) without expert consultation.

The treatment of MDRTB can be as complex as cancer chemotherapy and should not be attempted without the consultation of a specialist. Patients with MDRTB should be treated under a DOT program (see Point 6). Always use at least 2, and preferably 3 to 5, drugs to which the patient's organism is susceptible. Continue treatment for 18 to 24 months after culture conversion to negative. Monitor closely for adverse drug reactions and interactions (see Table 3). Assess drug absorption by monitoring serum drug levels, if possible.

TB HOTLINE 212-788-4162

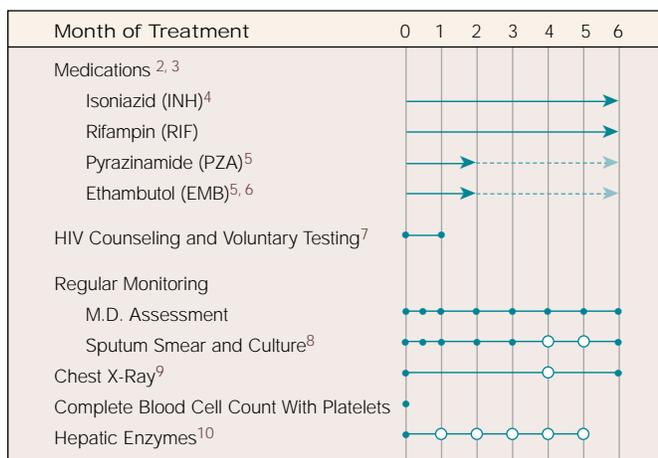
Table 1. — Countries and Areas With an Estimated or Reported High Incidence of TB, 1997
(Based on World Health Organization Regions)

Africa	All countries and areas except Algeria and Seychelles			
Eastern Mediterranean	Afghanistan Bahrain Djibouti Iran	Iraq Morocco Pakistan Saudi Arabia	Somalia Sudan Syrian Arab Republic Yemen	
Europe	Azerbaijan Belarus Bosnia-Herzegovina Croatia Estonia Georgia	Hungary Kazakhstan Kyrgyzstan Latvia Lithuania Macedonia	Moldova, Rep. of Poland Portugal Romania Russian Federation Spain	Tajikistan Turkmenistan Ukraine Uzbekistan Yugoslavia
North, Central, and South America	Argentina Bahamas Belize Bolivia Brazil	Colombia Dominican Republic Ecuador El Salvador Guatemala	Guyana Haïti Honduras Nicaragua Panama	Paraguay Peru Suriname
Southeast Asia	Bangladesh Bhutan India	Indonesia Maldives Myanmar (formerly Burma)	Nepal Sri Lanka Thailand	
Western Pacific	Brunei Darussalam Cambodia China, including Hong Kong Cook Islands Fiji French Polynesia Guam Kiribati	Korea, Republic of Lao People's Dem. Rep. Macao Malaysia Marshall Islands Micronesia, Fed. States of Nauru New Caledonia	Northern Mariana Islands Palau Papua New Guinea Philippines Samoa Singapore Solomon Islands Tonga	Tuvalu Vanuatu Viet Nam Wallis & Futuna

Notes

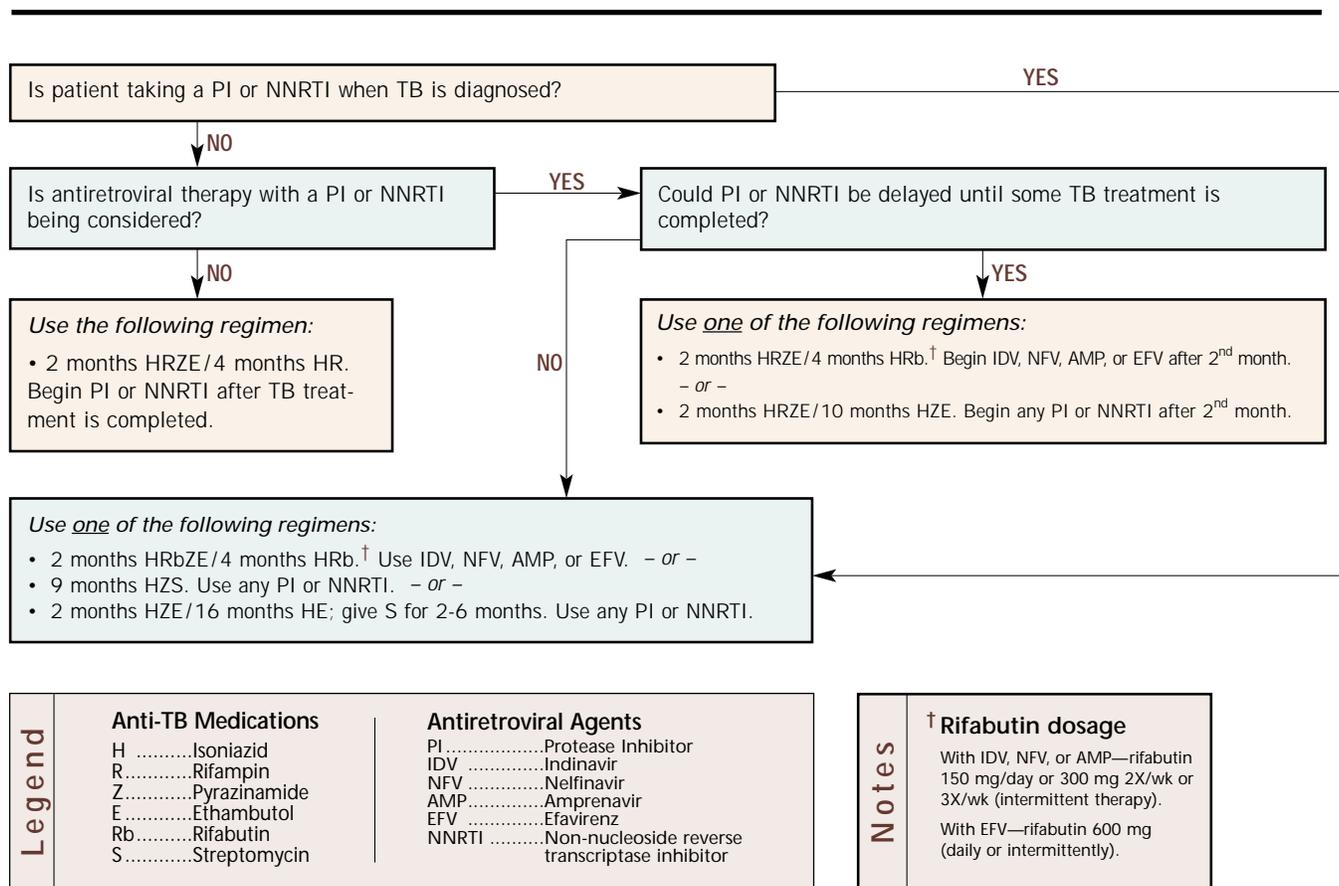
- Source: Global Tuberculosis Programme, World Health Organization. *Global Tuberculosis Control: WHO Report 1999*. Geneva: World Health Organization; 1999. "High-incidence areas" are defined by the New York City Bureau of Tuberculosis Control as areas with ≥20 estimated or reported smear-positive cases per 100,000 persons.
- Most countries and areas that are not listed should be considered low incidence (<20 smear-positive cases per 100,000 persons), based on estimated or reported rates. However, the following countries and areas should not necessarily be considered low incidence, because no data were available: Cayman Islands, Liechtenstein, Monaco, Montserrat, Niue, San Marino, Tokelau.

Table 2. — Therapy Timeline for Previously Untreated Tuberculosis Patients With Drug-Susceptible Active Disease¹



- All initial isolates of *M. tuberculosis* should have drug-susceptibility testing performed. *This chart applies only to patients whose isolates are found to be drug susceptible.* If drug resistance is documented, consult a physician expert in its management. Physicians may obtain information on prior treatment and susceptibility results from the Department of Health by calling (212) 788-4162 during business hours.
- Pending the results of drug susceptibility testing, begin all patients on all 4 of the anti-TB medications listed, unless there are absolute contraindications. All patients with pulmonary TB, regardless of HIV status, should be treated for 6 months or for 3 months beyond documented culture conversion, whichever is longer. HIV-seropositive patients who have a delayed clinical or bacteriologic response to treatment should be treated for 9 months. Longer courses of therapy are also recommended for patients with certain forms of extrapulmonary disease.
- Ideally, every TB patient should receive every dose of anti-TB medication on a program of directly observed therapy (DOT). Call the Health Department at (212) 442-9777 for help in arranging DOT for your patient.
- Pyridoxine hydrochloride (Vitamin B₆), 25 mg with each dose of INH, may decrease peripheral neuritis and CNS effects. Pyridoxine should be given with INH to patients who are pregnant, malnourished, or who use alcohol.
- Continue PZA until (a) at least 8 weeks of therapy have been given *and* (b) laboratory results document susceptibility to INH and RIF. Many authorities would continue PZA until sputum is AFB-smear negative. EMB should be continued until susceptibility to INH and RIF is documented. If cultures are negative or drug susceptibility results are not available, continue all 4 drugs for the duration of treatment.
- During treatment with EMB, monitor visual acuity and color vision monthly.
- HIV counseling and testing should be encouraged for all TB patients, ideally at the first or second clinical visit.
- Regular monitoring of sputum AFB smears and mycobacteriology cultures is essential. Most patients (e.g., patients on DOT, patients adherent to the treatment regimen, and patients with isoniazid- and rifampin-susceptible TB) need monthly sputum tests until cultures become negative—documented by 2 negative cultures taken at least 1 month apart. To document cure, a sputum test should be obtained at the end of treatment. If drug resistance is documented, seek expert consultation.
- Obtain chest X-ray after 4 months to document response to treatment only if initial cultures are negative.
- Baseline liver function tests (LFTs) should be done for all patients. Monthly LFTs should be done for the following patients:
 - Patients whose baseline LFT results were abnormal
 - Patients who are HIV seropositive, regardless of baseline LFT results
 - Patients who have a history of heavy alcohol ingestion, liver disease, or chronic hepatitis, regardless of baseline LFT results
 - Pregnant and postpartum women (up to 2 months after delivery) who are currently taking isoniazid and/or rifampin, regardless of baseline LFT results
 - Patients who currently inject drugs or who have documented chronic hepatitis B or C infection, regardless of baseline LFT results

Table 4. — Recommended Antituberculosis Treatment Regimens for HIV-Infected Persons With Drug-Susceptible Tuberculosis Disease



Legend	Anti-TB Medications	Antiretroviral Agents	Notes
	H Isoniazid R Rifampin Z Pyrazinamide E Ethambutol Rb Rifabutin S Streptomycin	PI Protease Inhibitor IDV Indinavir NFV Nelfinavir AMP Amprenavir EFV Efavirenz NNRTI Non-nucleoside reverse transcriptase inhibitor	

Table 5. — The Use of Anti-Tuberculosis Medications in Special Situations: Pregnancy, Tuberculosis Meningitis, and Renal Failure

Medication	Safety in Pregnancy ¹	Central Nervous System Penetration ²	Dosage in Renal Insufficiency ³
Isoniazid	Has been used safely ⁴	Good (20–100%)	No change
Rifampin	Has been used safely (isolated reports of malformations)	Fair Inflamed meninges (10–20%)	No change
Rifabutin	Use with caution (limited data on safety)	Good (30–70%)	No change
Pyrazinamide	Avoid (limited data on safety)	Good (75–100%)	Decrease dose/increase interval (use with caution)
Ethambutol	Has been used safely	Inflamed meninges only (4–64%)	Decrease dose/increase interval
Aminoglycosides (Streptomycin, Kanamycin, Amikacin)	Avoid ⁵ (associated with hearing impairment)	Poor ⁶	Decrease dose/increase interval ⁷
Capreomycin	Avoid ⁵ (limited data on safety)	Poor	Decrease dose/increase interval ⁷
Ciprofloxacin, Levofloxacin, Ofloxacin, Sparfloxacin	Do not use (teratogenic in laboratory animals)	Fair (5–10%) Inflamed meninges (50–90%)	Decrease dose/increase interval
Ethionamide	Do not use (premature labor, congenital malformations)	Good (100%)	No change
Cycloserine	Avoid (limited data on safety)	Good (50–100%)	Decrease dose/increase interval
Para-aminosalicylic acid (PASER [®])	Has been used safely	Inflamed meninges only (10–50%)	Incomplete data
Clofazimine	Avoid (limited data on safety)	Unknown	Probably no change

Notes

- As with all medications given during pregnancy, anti-TB medications should be used with extreme caution. The risk of TB to the fetus far outweighs the risk of medications. Data are limited on the safety of anti-TB medications during pregnancy. This table presents a consensus of published data and recommendations. For recommendations on preventive treatment and treatment of TB disease during pregnancy, see Reference 12.
- Steroid treatment appears to improve outcome in TB meningitis, particularly in patients with altered mental status.
- If possible, monitor serum drug levels of patients with renal insufficiency.
- Supplement with pyridoxine (vitamin B₆) during pregnancy.
- If an injectable medication must be used during pregnancy, streptomycin is preferred.
- Has been used intrathecally; efficacy not documented.
- Avoid aminoglycosides and capreomycin in patients with reversible renal damage, if possible.

Table 3. — Medications Used in the Treatment of Tuberculosis: Dosages, Major Adverse Reactions, and Recommendations

	Drug	Daily Dose [max]	Twice weekly dose ¹ [max]	Thrice weekly dose ¹ [max]	Major Adverse Reactions ²
FIRST-LINE MEDICATIONS	Isoniazid (INH) ³ PO or IM	C: 10mg/kg A: 300mg [300mg]	C: 20-40mg/kg A: 15mg/kg [900mg]	A: 15mg/kg [900mg]	Hepatic enzyme elevation; peripheral neuropathy; hepatitis; CNS effects; increased phenytoin (Dilantin [®]) levels; interaction with disulfiram (Antabuse [®]).
	Rifampin (RIF) ³ PO or IV	C: 10-20mg/kg A: 600mg [600mg]	C: 10-20mg/kg A: 600mg [600mg]	A: 600mg	Orange discoloration of secretions, urine, tears, and contact lenses. Hepatitis, fever, thrombocytopenia, flu-like syndrome. Reduces levels of many drugs, including methadone, warfarin, birth control pills, theophylline, dapsone, ketoconazole, protease inhibitors (PIs), and non-nucleoside reverse transcriptase inhibitors (NNRTIs).
	Pyrazinamide (PZA) ³ PO	C: 20-30mg/kg A: 1.5g (<50kg) 2g (51-74kg) 2.5g (75+kg)	C: 40-50mg/kg A: 2.5g (<50kg) 3g (51-74kg) 3.5g (75+kg)	A: 2.0g (<50kg) 2.5g (51-74kg) 3.0g (75+kg)	GI upset; hepatotoxicity; hyperuricemia; arthralgias; rash.
	Ethambutol (EMB) PO	C&A: 15-25mg/kg [2.5g]	C: 30-50mg/kg A: 50mg/kg	A: 30mg/kg	Decreased red-green color discrimination; decreased visual acuity; skin rash.
	Rifabutin ⁴ PO	C: 10-20mg/kg A: 5mg/kg [300mg]	C: 10-20mg/kg A: 5mg/kg [300mg]	Not known	Orange discoloration of secretions, urine, tears, and contact lenses. Rash; hepatitis; fever; neutropenia; thrombocytopenia. Reduced levels of many drugs including protease inhibitors (PIs) non-nucleoside reverse transcriptase inhibitors (NNRTIs), dapsone, ketoconazole, and birth control pills. Uveitis with high doses.
SECOND-LINE MEDICATIONS	Capreomycin ⁵ (CAP): IM/IV	C: 15-30mg/kg A: 15 mg/kg			Auditory, vestibular, and renal toxicity; eosinophilia; hypokalemia; hypomagnesemia.
	Ciprofloxacin ^{4,6} PO or IV	A: 750-1500mg			Abdominal cramps; GI upset; tremulousness; insomnia; headache; photosensitivity; drug interactions with warfarin and theophylline.
	Clofazimine ⁴ PO	C: 50-200mg A: 100-300mg			Orange/brown skin discoloration; GI complaints that can mimic appendicitis; rare visual disturbances.
	Cycloserine (CS) PO	C: 15-20mg/kg; A: 500-1000mg Divided doses			Psychosis; seizures; headache; depression; other CNS effects (give Vit. B ₆ 50mg per 250mg of CS); rash; increased phenytoin (Dilantin [®]) levels.
	Ethionamide: PO	C: 15-20mg/kg; A: 500-1000mg Divided doses			GI upset; bloating; hepatotoxicity; hypothyroidism (esp. with PAS); metallic taste.
	Kanamycin (KAN) ⁵ Amikacin: ⁴ IM/IV	C: 15-30mg/kg A: 15mg/kg			Auditory and renal toxicity; rare vestibular toxicity; hypokalemia; hypomagnesemia.
	Levofloxacin ^{4,6} PO or IV	A: 500-1000mg			Similar to ciprofloxacin but many fewer side effects and drug interactions.
	Ofloxacin: ^{4,6} PO or IV	A: 600-800mg			Probably similar to ciprofloxacin; possibly fewer drug interactions.
	Para-aminosalicylic acid (PASER [®]): PO	C: 150mg/kg A: 4g every 12 h [†]			GI disturbance; hypersensitivity; hepatotoxicity; hypothyroidism; decreased digoxin, increased phenytoin (Dilantin [®]) levels; levels decreased by diphenhydramine (Benadryl [®]).
	Sparfloxacin ^{4,6} PO	A: 200mg (first dose = 400mg)			Photosensitivity; prolongation of QT _c interval.
Streptomycin ^{5,7} (SMN): IM/IV	C: 20-30mg/kg A: 15mg/kg			Auditory and renal toxicity; hypokalemia; hypomagnesemia.	

Notes

(C) = Children (A) = Adults

1. Ideally, every patient with active TB should receive every dose of anti-TB medication on a program of directly observed therapy. Intermittent therapy, which should always be directly observed, can only be used in some clinical situations. Intermittent dosing of oral second-line medications is not recommended.

2. Not all toxicities are listed. Check package insert or pharmacology text for further information. Use of brand names does not imply endorsement of any product by the New York City Department of Health.

3. An INH/RIF combination tablet (Rifamate[®]) containing 150mg of INH and 300mg of RIF, and an INH/RIF/PZA combination (Rifater[®]) containing 50mg of INH, 120mg of RIF, and 300mg of PZA are available and should be used whenever patients are not on directly observed therapy.

Recommended Regular Monitoring

Recommended Regular Monitoring	Comments	
Hepatic enzymes (if baseline abnormal)	Overdose may be fatal. Aluminum-containing antacids reduce absorption. Pyridoxine hydrochloride (vitamin B ₆) may decrease peripheral neuritis and CNS effects.	FIRST-LINE MEDICATIONS
Hepatic enzymes (if baseline abnormal)	Single doses on empty stomach (2 hours before or after meals). Patients on methadone will need an increased dose of methadone (average 50%) to avoid opiate withdrawal. Interaction with many drugs leads to decreased levels of one or both. May make glucose control more difficult in diabetics. Contraindicated for patients taking PIs and most NNRTIs.	
Hepatic enzymes (if baseline abnormal)	May complicate management of diabetes mellitus. Hyperuricemia can be used as indicator of compliance. Treat increased uric acid only if symptomatic.	
Check color vision and visual acuity monthly	Optic neuritis may be unilateral; check each eye separately. If possible avoid in children too young to undergo vision testing.	
Complete blood cell count with platelets monthly; hepatic enzymes (if baseline abnormal)	Use adjusted daily dose of rifabutin, and monitor for decreased antiretroviral activity and for rifabutin toxicity if taken concurrently with PIs or NNRTIs. Contraindicated for patients taking ritonavir, saquinavir, or delavirdine.	
Audiometry, renal function, and electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.	SECOND-LINE MEDICATIONS
	Variable absorption; check serum levels if possible. Antacids/sucralfate reduce absorption. Caffeine effects may be increased.	
	Efficacy unproven. May cause acute abdominal pain mimicking appendicitis.	
Assessment of mental status	Increase gradually, checking serum levels. Pyridoxine hydrochloride (vitamin B ₆), 50 mg with each 250 mg, may decrease CNS effects. Monitor weekly blood levels until stable, if possible.	
Hepatic enzymes (if baseline abnormal); thyroid function	Antacids/anti-emetics and lying flat for 20 minutes after doses may help tolerance. Start with 250 mg daily and increase as tolerated.	
Audiometry, renal function, and electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.	
	Similar to ciprofloxacin.	
	Similar to ciprofloxacin.	
Thyroid function	Begin gradually and increase dosage as tolerated. May cause hemolytic anemia in patients with G6PD deficiency.	
EKG (if baseline abnormal)	Contraindicated for individuals taking disopyramide, amiodarone, and other QT _c prolonging antiarrhythmic drugs and in individuals with known QT _c prolongation. Minimize direct sunlight exposure while on sparfloxacin and for up to 5 days after discontinuation to avoid phototoxicity.	
Audiometry, renal function, and electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.	

4. Not FDA approved for the treatment of tuberculosis.

5. In persons older than 60 the daily dose of streptomycin should be limited to 10 mg/kg. For patients with drug-resistant isolates, injectable medications are generally given 5 days per week for several months, then reduced to 2-3 times per week, preferably after sputum cultures have become negative.

6. Should not be used for treatment of children.

7. Available from Pfizer Pharmaceuticals. Call (800) 254-4445.

† Berning SE, Huitt GA, Peloquin CA. Pharmacokinetics of p-aminosalicylic acid (PAS) granules dosed every 12 or 24 hours. *Am J Resp Crit Care Med.* 1998; 157(3):A467 [Abstract, American Thoracic Society International Conference, 1998].

8 Consider interactions with HIV medication when prescribing anti-TB regimens for HIV-infected individuals.

The Department of Health's current recommendation is to treat HIV-seropositive TB patients with a 6-month course of anti-TB therapy (see Table 2). In patients with a delayed response, treatment should be prolonged to 9 months. However, 2 new classes of antiretroviral drugs (protease inhibitors and non-nucleoside reverse transcriptase inhibitors) available for the treatment of HIV infection interact significantly with important anti-TB drugs, the rifamycins (e.g., rifampin, rifabutin). Expert consultation is recommended for decisions regarding antiretroviral therapy for a patient with tuberculosis (see Table 4 and References 6,7,8,12,13).

9 Prescribe treatment for TB infection when appropriate.

The purpose of treatment is to stop latent, asymptomatic TB infection from progressing to clinical disease and to prevent the recurrence of inadequately treated past disease. Taken correctly, treatment for TB infection reduces the risk of developing TB disease by as much as 90% or more—even in patients with HIV infection. The following individuals with a positive Mantoux tuberculin skin test reaction are candidates for treatment of TB infection, regardless of age:

- Close contacts of a person with pulmonary or laryngeal TB disease
- HIV-infected persons and persons at high risk for HIV infection whose HIV status is unknown
- Persons whose skin tests have converted recently (≥ 10 mm increase within a 2-year period)
- Persons with medical risk factors for TB disease other than HIV infection (e.g., diabetes, leukemia, Hodgkin's disease)
- Persons with radiographic evidence of old, healed TB and with no history of adequate treatment

Treatment of TB infection is also recommended for all patients who have a positive tuberculin skin test reaction and who are younger than 35 years (up to the 35th birthday), especially children younger than 5 years who have a ≥ 10 mm reaction. The standard regimen for the treatment of TB infection is INH given daily or weekly for 6 to 12 months, depending on age and HIV status. (See Reference 12 for alternative regimens to treat TB infection in HIV-seropositive patients.)

10 Decide if an alternative preventive treatment regimen for contacts of MDRTB cases is necessary.

If an individual is a contact to a case of MDRTB, the standard treatment regimen for TB infection will not be adequate. Before selecting an alternative treatment regimen for TB infection, clinicians should consider the contact's risk for MDRTB infection and disease. At least three factors should be considered:

- *How likely is it that the individual is newly TB-infected?* An individual with a documented prior positive tuberculin skin test reaction is less likely to be newly infected and is probably not a candidate for alternative regimens for TB infection.
- *How likely is the individual to develop active TB?* Contacts are at high risk of developing TB disease if they have been recently infected, if they are infants, or if they are HIV seropositive or otherwise immunosuppressed. Physicians should be aggressive in prescribing multidrug treatment of TB infection for these individuals.
- *How likely is it that the individual is infected with a strain of MDRTB?* Three factors should be considered: the infectiousness of the source patient, the closeness and intensity of the MDRTB exposure, and the contact's risk of exposure to drug-susceptible TB.

Before prescribing treatment for TB infection for a contact of a case of MDRTB, the drug susceptibility pattern of the source patient must be considered in the selection of medications for the treatment of latent TB infection (see Reference 5).

References and Additional Reading

1. American Thoracic Society, Centers for Disease Control. Control of tuberculosis in the United States. *Amer Rev Resp Dis.* 1992; 146:1623-1633.
2. American Thoracic Society, Centers for Disease Control. Treatment of tuberculosis infection in adults and children. *Amer Rev Resp Dis.* 1994; 149:1359-1374.
3. Centers for Disease Control and Prevention. *Core Curriculum on Tuberculosis* (3rd edition). Atlanta: U.S. Department of Health and Human Services, 1994.
4. Centers for Disease Control and Prevention. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. *MMWR.* 1994;43(RR-13).
5. Centers for Disease Control and Prevention. Management of persons exposed to multidrug-resistant tuberculosis. *MMWR.* 1992;41(RR-11).
6. Chaisson RE, Clermont HC, Holt EA, et al. Six-month supervised intermittent tuberculosis therapy in Haitian patients with and without HIV infection. *Am J Respir Crit Care Med.* 1996;154:1034-1038.
7. El-Sadr WM, Perlman DC, Matts JP, et al. Evaluation of an intensive intermittent-induction regimen and duration of short-course treatment for human immunodeficiency virus-related pulmonary tuberculosis. *Clin Infect Dis.* 1998;26:1148-1158.
8. Kassim S, Sassan-Morokro M, Ackah A, Abouya LY, Digbeu H, Yesso G. Two-year follow-up of persons with HIV-1 and HIV-2 associated pulmonary tuberculosis treated with short-course chemotherapy in West Africa. *AIDS.* 1995;9:1185-1191.
9. New York State Department of Health. Control of tuberculosis in hospitals. Albany, NY: New York State Department of Health memorandum no. 927, March 13, 1992.
10. New York City Department of Health. Preventive treatment for tuberculosis. CITY HEALTH INFORMATION. 1995;14,3:1-4.
11. New York City Department of Health. Skin testing for tuberculosis. CITY HEALTH INFORMATION. 1997;16,1:1-4.
12. New York City Department of Health, Bureau of Tuberculosis Control. *Clinical Policies and Protocols.* 3rd edition. June 1999.
13. New York City Department of Health, Bureau of Tuberculosis Control. TB Fact Sheet 2j [revised]. Antiretroviral drugs and the treatment of tuberculosis. Rev. 1/99.

Acknowledgment.—Paula I. Fujiwara, M.D., M.P.H., Assistant Commissioner, and Sonal Munsiff, M.D., Director of Epidemiology and Surveillance, Bureau of Tuberculosis Control. Appreciation is expressed to Pamela Kellner, R.N., M.P.H., Director of Program Development, for cover art reproduced from Kimber DC, Gray CE, *Text-Book of Anatomy and Physiology for Nurses*, 4th ed., New York, NY: The Macmillan Company, 1917:239.

Recommendation Updates

- For most patients with isoniazid- and rifampin-susceptible tuberculosis, it is not necessary to examine sputum monthly once culture conversion is documented (i.e., 2 negative cultures taken at least 1 month apart). However, sputum should be taken at the end of treatment to document cure (see Point 5 and Table 2).
- A 6-month regimen is now recommended for the treatment of pulmonary TB disease in HIV-infected individuals. (Previously, the Department of Health recommended a 9-month regimen for these patients.) However, the final decision on the length of treatment for HIV-infected patients should depend on the patient's clinical and bacteriologic response to treatment (see Point 8 and Table 2).
- Guidelines have been developed for the TB treatment of patients who have started or may start treatment with protease inhibitors and non-nucleoside reverse transcriptase inhibitors (see Point 8 and Table 4).
- Two new fluoroquinolones, sparfloxacin (Zagam[®]) and levofloxacin (Levaquin[®]) have been added to the treatment recommendation for patients with TB strains that are drug resistant or patients with drug intolerances. Also, rifabutin has also been added to the treatment recommendations for patients on antiretroviral therapy (see Tables 3, 4, and 5).

A Directory of Tuberculosis-Care Resources

The New York City Department of Health

Reporting

TB Hotline for Physicians(212) 788-4162

To report a suspected or confirmed case of tuberculosis and to obtain information on the treatment and drug susceptibility of your TB patient.

Fax.....(212) 788-4179

Directly-Observed Therapy

Information.....(212) 442-9777

Assistance in arranging a program for your patient.

Laboratory Services

Mycobacteriology Reference

Laboratory(212) 447-6745

To submit specimens and cultures and to obtain test results of previous submissions.

Education

Information.....(212) 442-9968

For questions about tuberculosis, for copies of Department of Health publications, and to obtain training information and educational materials in English, Spanish, Haitian Creole, Russian, and Chinese.



Chest Clinics

Free, confidential, state-of-the-art care for patients with tuberculosis, their contacts, and other persons at risk for TB infection. Hours may change; call to confirm.

Bronx

Morrisania Chest Center(718) 901-6536, 6538

1309 Fulton Avenue, Bronx, NY 10456

Monday–Friday 8:00 a.m.–5:30 p.m.

Saturday 8:30 a.m.–4:30 p.m.

Fax(718) 590-6736

Brooklyn

Bedford(718) 574-2462, 2463

485 Throop Avenue, Brooklyn, NY 11221

Monday–Friday 8:30 a.m.–4:30 p.m.

2nd and 4th Saturday of every month

8:30 a.m.–4:30 p.m.

Fax(718) 455-1895

Brownsville(718) 495-7256, 7258

259 Bristol Street, Brooklyn, NY 11212

Monday–Friday 8:30 a.m.–5:00 p.m.

Fax(718) 346-8255

Bushwick(718) 573-4886, 4891

335 Central Avenue, Brooklyn, NY 11221

Tuesday, Wednesday, and Thursday

8:30 a.m.–4:30 p.m.

Fax(718) 573-4899

Fort Greene(718) 643-8357, 6551

295 Flatbush Avenue Extension, Brooklyn, NY 11201

Monday and Thursday 8:30 a.m.–7:00 p.m.

Tuesday, Wednesday, and Friday, 8:30 a.m.–5:00 p.m.

Saturday 8:30 a.m.–4:30 p.m.

Fax(718) 643-6367

Manhattan

Chelsea(212) 239-1749, 1757

303 Ninth Avenue, New York, NY 10001

Monday and Thursday 8:30 a.m.–7:00 p.m.

Tuesday, Wednesday, and Friday 8:00 a.m.–5:00 p.m.

2nd and 4th Saturday of every month

8:30 a.m.–4:30 p.m.

Fax(212) 290-2324

Washington Heights Chest Center ..(212) 304-5435

600 W. 168th Street, New York, NY 10032

Monday–Thursday 8:30 a.m.–6:00 p.m.

Friday 8:30 a.m.–5:00 p.m.

1st and 3rd Saturday of every month

8:30 a.m.–4:30 p.m.

Fax(212) 740-9162

Queens

Corona.....(718) 476-7635, 7636

34-33 Junction Boulevard, Jackson Heights, NY 11372

Monday and Thursday 8:00 a.m.–7:00 p.m.

Tuesday, Wednesday, and Friday 8:00 a.m.–5:00 p.m.

Saturday 8:30 a.m.–4:30 p.m.

Fax(718) 476-7818

Far Rockaway(718) 474-2100, 2101

67-10 Rockaway Beach Boulevard, Far Rockaway, NY 11692

Monday 8:30 a.m.–12:30 p.m.

Friday 8:30 a.m.–4:30 p.m.

Fax(718) 945-2596

Staten Island

Richmond(718) 983-4530

51 Stuyvesant Place, Staten Island, NY 10301

Monday–Friday 8:30 a.m.–4:30 p.m.

Fax(718) 983-4529

The National Jewish Center for Immunology & Respiratory Medicine

Information.....(800) 423-8891

Clinical ConsultationExt. 1279

Mycobacteriology.....Ext. 1339

PharmacokineticsExt. 1925



THE DOUBLE RED CROSS
International Emblem of the
Campaign Against Tuberculosis