



City Health Information

December 2003

The New York City Department of Health and Mental Hygiene

Vol. 22 No. 7

TUBERCULOSIS TREATMENT

TB IS CURABLE!

- Think TB! in any patient with chronic cough and fever, especially if the person has a risk factor for TB.
- Obtain specimens for culture and drug susceptibility.
- Start treatment with a four-drug regimen.
- Ensure treatment completion by using Directly Observed Therapy.

The principal strategy for controlling tuberculosis (TB) is to promptly identify individuals with infectious TB, and then quickly and permanently render them non-infectious through effective treatment.

The treatment of TB is beneficial to the individual and to the community as a whole by reducing TB transmission. Physicians who properly treat TB and ensure successful completion of therapy are therefore performing an essential public health service.

The first edition of *City Health Information* "Tuberculosis Treatment" was published in 1992. This fourth edition contains updated tables and figures, based on the recently published national TB treatment guidelines of the American Thoracic Society, the Centers for Disease Control and Prevention (CDC), and the Infectious Diseases Society of America.¹

What's new in the national TB guidelines:¹

- Patient-centered case management, with an adherence plan that emphasizes Directly Observed Therapy (DOT), as the initial treatment strategy;
- Rifapentine and isoniazid once weekly in the continuation phase of treatment (months 3–6) for selected HIV-negative patients;
- Sputum cultures should be obtained at the end of the intensive phase of treatment (end of month 2) to identify those at increased risk of subsequent relapse. If culture(s) is positive, the continuation phase of treatment should be prolonged for selected individuals.

The new national guidelines clearly assign responsibility for successful treatment to the private provider and the public health program, *not* to the patient.¹ Physicians should ensure that every TB treatment plan stresses the use of DOT. For patients with drug-susceptible TB, providers should use intermittent regimens to facilitate the provision of DOT.

To achieve TB treatment goals, both physicians and

the NYC Department of Health and Mental Hygiene (NYC DOHMH) Bureau of TB Control need to increase their commitment to working together as partners. By coordinating care with local public health authorities, physicians are more likely to achieve better outcomes for their patients.

The following recommendations should always be a part of TB clinical care:

- Standard 6-month treatment (short course chemotherapy) consists of a 2-month intensive phase followed by a 4-month continuation phase.
- Initial isolate of *Mycobacterium tuberculosis* (*M. tb*) should be submitted for drug-susceptibility testing.
- Sputum should be obtained at least monthly until culture conversion to negative has been documented. Also obtain sputum sample(s) at the end of the intensive phase of treatment and at the completion of treatment to document cure.
- Patients should be evaluated monthly for adherence and adverse reactions to therapy. The drug regimen should be modified based on drug-susceptibility patterns.
- A single drug should *NEVER* be added to a failing regimen.
- Treatment of multidrug-resistant tuberculosis (MDRTB) — disease with *M. tb* resistant to isoniazid and rifampin — should not be attempted without consulting an expert.
- Special attention should be given to individuals who have both TB and HIV/AIDS, as certain antiretroviral drugs may complicate TB treatment. Seeking expert advice is essential to the optimal management of patients with both diseases.^{2,3}

Physicians are required by law to report all suspected or confirmed cases of TB and their contacts to the NYC DOHMH.^{4,5} Call 311 or (212) 788-4162 to access the Department's TB Hotline for Physicians.

Ten Basics on TB Diagnosis, Treatment, and Prevention

1 Think TB!

Consider the diagnosis of active TB in any patient with chronic cough and fever, especially if the person has risk factors for TB disease. The following individuals are at increased risk for TB disease:

- Close contacts of a person with pulmonary or laryngeal TB;
- Individuals infected with HIV;
- Individuals with medical risk factors other than HIV infection (e.g., organ transplant, diabetes, leukemia, Hodgkin's disease, immunosuppressive or corticosteroid therapy);
- Individuals with radiographic evidence of old, healed TB;
- Immigrants from countries with a high incidence of TB;
- Employees or residents of hospitals, correctional facilities, homeless shelters, or nursing homes;
- Injecting drug users;
- Individuals whose tuberculin skin tests (TSTs) have converted to positive within the past 2 years.

2 Report suspected or confirmed cases of active TB to the NYC DOHMH.

Medical providers, infection-control practitioners, and laboratories are required by law to report all suspected and confirmed cases of TB to the NYC DOHMH within 24 hours of suspected diagnosis (See Reporting Table).^{4,5}

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

Take a complete history of prior TB treatment; patients with active TB who have undergone treatment previously are more likely to have drug-resistant disease. As patients may not know if the treatment they received in the past was for TB disease, it is important to ask questions that will elicit such history; (i.e., have they ever taken medicine that turned their urine red-orange [rifampin], or have they ever received injections over a period of weeks or months [streptomycin]?).

Use rapid diagnostic tests for TB that have been approved by the FDA, such as the Roche Polymerase Chain Reaction (PCR) test (Amplicor®)* and the amplified *Mycobacterium Tuberculosis* Direct test (MTD®)*, for acid-fast bacilli (AFB) smear-positive and smear-negative respiratory specimens.²

The NYC DOHMH maintains a registry of patients with active TB in New York City consisting of each patient's treatment history as well as bacteriology and

drug-susceptibility test results. The New York State Sanitary Code requires susceptibility testing be performed on all initial isolates of *M. tb*.⁵

4 Begin treatment with at least four anti-TB drugs for any patient who has not been previously treated for TB.

Rates of isoniazid resistance remain high in New York City.⁶ Use of a four-drug empiric regimen reduces the chance of further drug resistance. Therefore, patients with active TB who have never been treated before for the disease should be started on isoniazid, rifampin, pyrazinamide, and ethambutol. In the continuation phase, isoniazid and rifampin should be given for 2 months if initial cultures are negative, for a total of 4 months of treatment. The continuation phase should last for 4 months (a total of 6 months of treatment) if initial cultures were positive but susceptibility results are not available. Pyrazinamide and ethambutol can be discontinued at the end of the intensive phase of treatment in both situations, unless drug resistance is strongly suspected. If vision testing cannot be reliably performed, as in very young children, ethambutol should be excluded from the initial regimen (See Timeline and Primary/Reserve Medications Tables).

Never Add A Single Drug To A Failing Regimen. To do so may promote further drug resistance. If MDRTB is suspected, consult an expert.

5 Provide ongoing TB care.

TB care is complex and should 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 Bureau of TB Control chest center for consultation, ongoing care, and medications at no cost to the patient. In addition, physicians can obtain expert medical consultation by calling 311 or (212) 442-9968 and asking for the physician on call in the NYC DOHMH Bureau of TB Control.

Important aspects of TB care:

- Since immune status can be a critical factor in treatment outcome, voluntary and confidential HIV counseling and testing should be offered to all patients.
- Patients should be thoroughly evaluated at the first clinical visit, then monitored at least monthly to assess for adverse reactions, adherence, and response to treatment (See Primary/Reserve Medications Tables). Only a 1-month supply of medication should be prescribed at a time. The treatment regimen usually needs to be modified based on drug-susceptibility results after the 2-month intensive phase of treatment.

- A 7-month continuation phase is recommended for: (1) patients with cavitary TB whose sputum culture is positive at the end of the intensive phase of treatment and (2) patients who did not receive pyrazinamide during the intensive phase of treatment (See Timeline Figure).
- Most patients with isoniazid- and rifampin-susceptible pulmonary TB need monthly sputum tests only until cultures convert to negative (documented by two negative cultures taken 2–4 weeks apart). Continue to monitor on a monthly basis patients who have drug-resistant TB or who are on non-standard regimens. Obtain sputum specimens to document cure at completion of treatment from all initially culture-positive patients with pulmonary TB.
- Baseline hepatic enzymes, blood urea nitrogen and creatinine, and a complete blood count should be obtained for all patients. Follow-up liver function tests are necessary only for selected individuals (See Timeline Figure).
- If a patient develops symptoms consistent with liver injury, medications should be held and the patient should be evaluated *immediately*.
- If sputum cultures remain positive after 4 months of treatment, explore the possibility of patient nonadherence to treatment or the presence of drug-resistant TB. Only after both of these scenarios are excluded should malabsorption be considered the cause of poor response.

6 Give top priority to completion of treatment.

A treatment completion strategy should be formulated immediately upon diagnosis. Ideally, every TB patient should receive every dose of anti-TB medication through a program of DOT, in which a health care worker watches the patient take the medication. Without observation of treatment, many patients stop treatment before they are cured. When this occurs, patients remain ill and can continue to infect others. Such patients are also more likely to develop MDRTB, a potentially deadly form of the disease. Most patients can complete treatment within 6–9 months, regardless of site of disease. Treatment should not be prolonged unnecessarily.

DOT can be provided either at a NYC DOHMH chest center or by outreach workers who meet a patient at his or her home, workplace, or another designated location. To arrange DOT for your patient and to obtain free medications via the “gratis meds” program, call 311 or (212) 442-9968 to access the NYC DOHMH Bureau of TB Control.

7 Who is eligible for the new once-a-week regimen?¹

The latest national guidelines recommend a new treatment option for patients 12 years of age or older with drug-susceptible pulmonary TB who are not infected with HIV: **rifapentine and isoniazid given once per week under DOT in the continuation phase of treatment.**

A patient must have the following: (i) culture-positive, drug-susceptible pulmonary TB; (ii) HIV-negative status; (iii) no cavitation present on initial chest radiograph; and (iv) documented negative sputum smear by the end of the 2-month intensive phase of treatment that includes at least rifampin, isoniazid, and pyrazinamide. The results of a sputum smear should be available before deciding upon a continuation phase regimen. If a patient meets all of these criteria, the isoniazid and rifapentine regimen is preferred. If the sputum culture has not converted to negative at the end of the 2-month intensive phase, treatment should be extended for an additional 3 months, i.e., 9 months of therapy in total (See Rifapentine Figure).

8 Never treat MDRTB without consulting an expert.

The treatment of MDRTB can be as complex as cancer chemotherapy and should not be attempted without consulting a specialist. Patients with MDRTB should always be treated under a DOT program. Always use at least two — preferably three to five — drugs to which the patient’s organism is susceptible, and continue treatment for 18–24 months after cultures convert to negative. Monitor patients closely for adverse drug reactions and interactions.

9 Be alert to drug interactions when HIV and TB medications are used together.

Many antiretroviral drugs (protease inhibitors and non-nucleoside reverse transcriptase inhibitors) used to treat HIV infection have clinically significant interactions with the rifamycins (e.g., rifampin, rifabutin, rifapentine), key anti-TB drugs. The NYC DOHMH recommends that physicians consult with an expert regarding antiretroviral therapy for patients with TB.^{1,2,3} In general, duration of treatment for HIV-infected patients is the same as that for non-HIV-infected individuals (See HIV Figure).

10 Treat latent TB infection (LTBI).

If completed, treatment for LTBI reduces the risk of developing active TB by as much as 90%, even in persons with HIV infection.⁷ LTBI treatment should be given both to individuals with suspected recent infection and individuals with conditions that increase the risk of progression from LTBI to active TB.⁷

The standard LTBI treatment regimen is isoniazid given daily (or two times per week under DOT) for 9 months.^{7,8} However, for a contact of a person with isoniazid-resistant TB or MDRTB, the standard LTBI treatment regimen — isoniazid — will be inadequate. In such cases, clinicians should consider the risk of infection with a resistant isolate. When selecting an alternative regimen, utilize the result of the drug susceptibility of the isolate from the source patient, if possible, in determining a regimen for the contact.²

*Use of brand names is for informational purposes only and does not imply endorsement by the New York City Department of Health and Mental Hygiene.

RESOURCES

TB CARE

The New York City Department of Health and Mental Hygiene

Reporting

TB Hotline for Physicians(212) 788-4162
To report a suspected or confirmed case of TB and to obtain information on the treatment and drug susceptibility of your TB patient.
Fax.....(212) 788-4179

Directly Observed Therapy

Information(212) 442-9968
Assistance in arranging a program for your patient and in obtaining free medications.

Laboratory Services

Mycobacteriology Reference Laboratory(212) 447-6745
To submit specimens and cultures for rapid diagnostic tests and drug susceptibility and to obtain test results of previous submissions.

Education

Information(212) 442-9968
www.nyc.gov/health/tb
For questions about TB, for copies of Department of Health and Mental Hygiene publications, and to obtain training information and educational materials in English, Spanish, Haitian Creole, Russian, and Chinese.

Chest Centers

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

BRONX

Morrisania(718) 579-4157, 4163
1309 Fulton Avenue, Bronx, NY 10456
Monday–Thursday 8:00 a.m.–5:30 p.m., Friday 8:30 a.m.–12:00 p.m.
1st and 3rd Saturday of every month 8:30 a.m.–4:30 p.m.
Fax.....(718) 410-0478

BROOKLYN

Bedford(718) 574-2462, 2463
485 Throop Avenue, Brooklyn, NY 11221
Monday, Tuesday, Friday 8:30 a.m.–4:30 p.m.
Wednesday 8:30 a.m.–12:00 p.m.
1st Saturday of every month 8:30 a.m.–4:30 p.m.
Fax.....(718) 455-1895

Brownsville(718) 495-8281, 7258
259 Bristol Street, Brooklyn, NY 11212
Monday–Thursday 8:30 a.m.–4:30 p.m.
Friday 8:30 a.m.–12:00 p.m.
Fax.....(718) 495-8448

Bushwick(718) 573-4886, 4891
335 Central Avenue, Brooklyn, NY 11221
Monday–Thursday 8:30 a.m.–4:30 p.m.
Friday 8:30 a.m.–12:00 p.m.
Fax.....(718) 573-4899

Fort Greene(718) 643-8357, 8358
295 Flatbush Avenue Extension, Brooklyn, NY 11201
Monday and Thursday 8:30 a.m.–7:00 p.m.
Tuesday and Wednesday 8:30 a.m.–5:00 p.m.
Friday 8:30 a.m.–12:00 p.m., Saturday 8:30 a.m.–4:30 p.m.
Fax.....(718) 643-6367

MANHATTAN

Chelsea(212) 239-1757, 0919
303 Ninth Avenue, New York, NY 10001
Monday and Thursday 8:30 a.m.–7:00 p.m.
Tuesday and Wednesday 8:30 a.m.–5:00 p.m.
Friday 8:30 a.m.–12:00 p.m.
2nd and 4th Saturday of every month 8:30 a.m.–4:30 p.m.
Fax.....(212) 290-2324

Washington Heights.....(212) 368-4500
600 W. 168th Street, New York, NY 10032
Monday–Thursday 8:30 a.m.–6:00 p.m., Friday 8:30 a.m.–12:00 p.m.
1st and 3rd Saturday of every month 8:30 a.m.–4:30 p.m.
Fax.....(212) 368-0338

QUEENS

Corona(718) 476-7635, 7636
34-33 Junction Boulevard, Jackson Heights, NY 11372
Monday and Thursday 8:30 a.m.–7:00 p.m.
Tuesday and Wednesday 8:30 a.m.–5:00 p.m.
Friday 8:30 a.m.–12:00 p.m.
Saturday 8:30 a.m.–4:30 p.m.
Fax.....(718) 476-7131

Far Rockaway.....(718) 474-2100, 2101
67-10 Rockaway Beach Boulevard,
Far Rockaway, NY 11692
Monday and Friday 8:30 a.m.–4:30 p.m.
Fax.....(718) 945-2596

STATEN ISLAND

Richmond.....(718) 420-1028
51 Stuyvesant Place, Staten Island, NY 10301
Monday, Wednesday, Friday 8:30 a.m.–4:30 p.m.
Fax.....(718) 273-8195

The National Jewish Center for Immunology & Respiratory Medicine

Information(800) 423-8891
Clinical Consultation.....Ext. 1279
Mycobacteriology.....Ext. 1339
Pharmacokinetics.....Ext. 1925

TB INFORMATION

American Thoracic Society (ATS)
www.thoracic.org
Centers for Disease Control and Prevention (CDC)
www.cdc.gov/nchstp/tb
www.findtbresources.org
International Union Against TB and Lung Disease (IUATLD)
www.iuatld.org
World Health Organization (WHO)
www.who.int/health_topics/tuberculosis/en/

MEDICAL RESERVE CORPS/NYC Please note: the correct web address for more information on the Medical Reserve Corps/NYC is www.medicalreserve.org, and the telephone number is (866) NYC-DOH1/(866) 692-3641.



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TREATING TB WITH RIFAPENTINE

Case of TB (≥ 12 years of age) with all of the following:

- Pan-sensitive organism
- Non-cavitary lesion(s) on CXR
- Pulmonary disease without extrapulmonary component

Yes

Obtain HIV test results

Unknown¹ or Positive

Negative

Sputum smear **NEGATIVE** at 2 months²

No

Yes

Once-weekly treatment³ (RPT 600 mg and INH 900 mg by DOT) after the 2-month intensive phase of at least INH, RIF, PZA

Sputum culture **NEGATIVE** by the end of 2-month intensive phase

Yes

Treat for a total of 6 months with at least 18 doses of INH and RPT during the continuation phase

No

Extend INH and RPT treatment by an additional 3 months, for a total of 9 months

Base treatment on drug-susceptibility results, as per NYC DOHMH and CDC/ATS/IDSA guidelines

Treat with either a RIF- or RBT-based regimen⁴
The standard regimen in the continuation phase is INH and RIF daily or two or three times per week for 4 months⁴

Notes

1. HIV counseling and testing is recommended.
2. A sputum smear should be performed 1 to 2 weeks prior to the end of the 2-month intensive phase.

3. Intermittent therapy should only be given under Directly Observed Therapy (DOT).
4. RIF or RBT should not be given biweekly to HIV-infected patients with CD4 counts <100 ; such patients should receive a daily regimen in the intensive phase and either daily or three times per week in the continuation phase.

LEGEND

Anti-TB Medications

EMB Ethambutol
INH Isoniazid
PZA Pyrazinamide
RBT Rifabutin
RIF Rifampin
RPT Rifapentine
SMN Streptomycin

Antiretroviral Agents

ABC Abacavir
AMP Amprenavir
TAZ Atazanavir
EFV Efavirenz
fos-AMP fos-Amprenavir
IDV Indinavir
LPV/r Lopinavir/ritonavir
NFV Nelfinavir
NNRTI Non-nucleoside reverse transcriptase inhibitor
NVP Nevirapine
PI Protease Inhibitor
ZDV Zidovudine
3TC Lamivudine

THE USE OF ANTI-TB DRUGS DURING PREGNANCY, TB MENINGITIS, AND RENAL AND HEPATIC FAILURE

DRUG	Safety in Pregnancy ¹	Central Nervous System Penetration ²	Dosage in Renal Insufficiency ³	Dosage in Hepatic Insufficiency
Isoniazid	Has been used safely ⁴	Good (20–100%)	No change	No change, but use with caution
Rifampin	Has been used safely (isolated reports of malformations)	Fair Inflamed meninges (10–20%)	No change	No change, but use with caution
Rifapentine	Safety not established	Not established	Not established	No change, but use with caution ⁵
Rifabutin	Use with caution (limited data on safety)	Good (30–70%)	No change	No change, but use with caution ⁵
Pyrazinamide	Recommended by WHO, ⁶ not by US FDA ⁷ (limited data on safety)	Good (75–100%)	Decrease dosage/increase interval (use with caution)	No change, but use with caution
Ethambutol	Has been used safely	Inflamed meninges only (4–64%)	Decrease dosage/increase interval	No change
Aminoglycosides (streptomycin, kanamycin, amikacin)	Avoid ⁸ (associated with ototoxicity in fetus)	Poor ⁹	Decrease dosage/increase interval ¹⁰	No change
Capreomycin	Avoid ⁸ (limited data on safety)	Poor	Decrease dosage/increase interval ¹⁰	No change
Ciprofloxacin, Levofloxacin, Moxifloxacin, Ofloxacin	Do not use (teratogenic in laboratory animals)	Fair (5–10%) Inflamed meninges (50–90%)	Decrease dosage/increase interval	No change, but use with caution
Ethionamide	Do not use (premature labor, congenital malformations)	Good (100%)	No change, but use with caution	No change, but use with caution
Cycloserine	Use with caution (limited data on safety)	Good (50–100%)	Decrease dosage/increase interval	No change
Para-aminosalicylic acid	Has been used safely	Inflamed meninges only	Likely no change, but use with caution	No change, but use with caution

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 most medications. Data are limited on the safety of anti-TB medications during pregnancy. This table presents a consensus of published data and recommendations.
- 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 hydrochloride (vitamin B6), 25 mg per day.
- Start with regular dosage and monitor serum drug concentration in hepatic insufficiency.
- World Health Organization
- US Food and Drug Administration
- If an injectable medication must be used during pregnancy, streptomycin is preferred.
- Has been used intrathecally; efficacy not documented.
- If possible, avoid aminoglycosides and capreomycin in patients with reversible renal damage.

LEGEND

Anti-TB Medications

EMB Ethambutol
 INH Isoniazid
 PZA Pyrazinamide
 RBT Rifabutin
 RIF Rifampin
 RPT Rifapentine
 SMN Streptomycin

Antiretroviral Agents

ABC Abacavir
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 IDV Indinavir
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 NFV Nelfinavir
 NNRTI Non-nucleoside reverse transcriptase inhibitor
 NVP Nevirapine
 PI Protease Inhibitor
 ZDV Zidovudine
 3TC Lamivudine

TREATMENT OPTIONS FOR HIV-INFECTED PATIENTS WITH TB¹

Is the patient taking a PI or NNRTI when diagnosed with TB?

Yes

Use **ONE** of the following regimens:

- 2 months INH, RIF, PZA, EMB then 4 months INH, RIF with an EFV-based (non-PI) regimen²

OR

- 2 months INH, RBT, PZA, EMB then 4 months INH, RBT³
Use IDV, NFV, AMP, LPV/r, fos-AMP, TAZ, NPV, or EFV

OR

- 9 months INH, PZA, SMN
Use any PI or NNRTI.

No

If PI or NNRTI is being considered, can treatment be delayed until after the 2-month intensive phase of TB treatment?

No

Yes

Use **ONE** of the following regimens:

- 2 months INH, RIF, PZA, EMB then 4 months INH, RBT³
Begin IDV, NFV, AMP, LPV/r, fos-AMP, TAZ, NVP, or EFV after 2nd month⁴

OR

- 2 months INH, RIF, PZA, EMB then 4 months INH, RIF
Begin EFV-based (non-PI) regimen after 2nd month²

OR

- 2 months INH, RIF, PZA, EMB then 10 months INH, PZA, EMB
Begin any PI or NNRTI after 2nd month.⁴

Notes

1. HIV-infected patients with a CD4 count < 100 should receive a daily regimen in the intensive phase and either daily or 3 times per week in the continuation phase.
2. With RIF, EFV daily dosage may need to be increased to 800 mg.
3. RBT dosage and frequency vary depending on the PI or NNRTI being used.
With EFV: RBT 450–600 mg (either daily or 2 or 3 times per week).
With NVP: RBT 300 mg (either daily or 2 or 3 times per week).
With IDV, NFV, AMP, TAZ, or fos-AMP: RBT 150 mg daily or 300 mg 2 or 3 times per week.
With LPV/r: RBT 150 mg every other day or 3 times per week. Other anti-TB drugs should be given daily in the intensive phase for patients with a CD4 count < 100.
4. There should be a 2-week washout period after the discontinuation of RIF and before starting a PI or NNRTI.

LEGEND

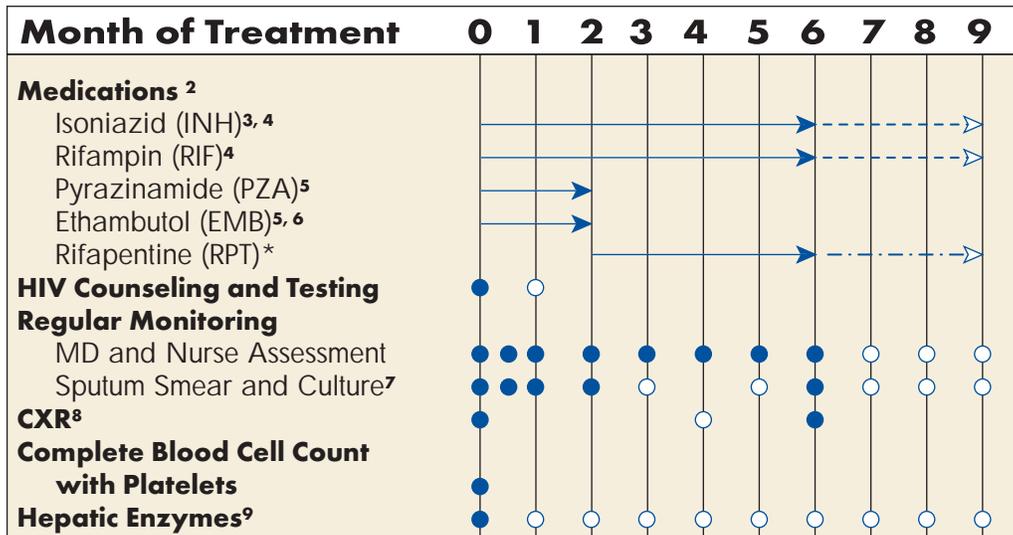
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IDV Indinavir	3TC Lamivudine
LPV/r Lopinavir/ritonavir		

THERAPY EVALUATION TIMELINE FOR PREVIOUSLY UNTREATED TB PATIENTS WITH DRUG-SUSCEPTIBLE ACTIVE DISEASE¹



* If rifapentine is used, rifampin should not be used.

● Recommended intervention

○ As needed

---> Continue treatment if PZA was not used in the intensive phase, if patient had a cavitary CXR and a positive sputum culture at the end of the intensive phase of treatment or received RPT and had a positive sputum culture at the end of the intensive phase.

- - -> If sputum cultures are positive at the end of the 2-month intensive phase, continue INH and RPT for 3 additional months (for a total of 9 months).

Notes

- 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. To obtain treatment information and susceptibility results, call (212) 788-4162 during business hours.
- Pending the results of drug-susceptibility testing, begin all patients on the first four anti-TB medications listed, unless there are absolute contraindications.
- Pyridoxine hydrochloride (vitamin B₆), 10–25 mg with each dose of INH, may decrease peripheral neuritis and CNS effects. Pyridoxine should be given with INH to selected patients.
- In the continuation phase, INH and RIF should be given for only 2 months if initial cultures are negative, for a total of 4 months of treatment. The continuation phase should last for 4 months (a total of 6 months of treatment) if initial cultures were positive but susceptibility results are not available.
- PZA and EMB can be discontinued for all patients with negative cultures at the end of the intensive phase of treatment and for those patients for whom drug-susceptibility results are not available, unless drug resistance is strongly suspected.
- During treatment with EMB, monitor visual acuity and color vision monthly.
- Most patients (e.g., patients on DOT, patients adherent to the treatment regimen, and patients with INH- and RIF-susceptible TB) need monthly sputum tests only until cultures become negative — documented by 2 negative cultures taken 2–4 weeks apart. To document cure, a sputum test should be obtained at the end of treatment. If drug resistance is suspected or documented, seek expert consultation.
- Obtain chest x-ray after 4 months to document response to treatment if initial cultures are negative. Chest x-ray should be obtained at the end of treatment as a baseline in the event of symptoms in the future.
- Baseline liver function tests (LFTs) should be done for all patients. Monthly LFTs should be done for patients:
 - Whose baseline LFT results were abnormal;
 - Who are HIV seropositive, regardless of baseline LFT results;
 - Who have a history of heavy alcohol ingestion, liver disease, or chronic hepatitis, regardless of baseline LFT results;
 - Who are pregnant or postpartum (up to 2 months after delivery) and are currently taking INH and/or RIF, regardless of baseline LFT results;
 - Who currently inject drugs or who have documented chronic hepatitis B or C infection, regardless of LFT results.

LEGEND

Anti-TB Medications

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fos-AMP fos-Amprenavir	ZDV Zidovudine
IDV Indinavir	3TC Lamivudine
LPV/r Lopinavir/ritonavir		

PRIMARY MEDICATIONS USED IN THE TREATMENT OF TB: DOSAGES, MAJOR ADVERSE REACTIONS, AND RECOMMENDED REGULAR MONITORING

DRUG <i>Route of Administration</i> MODE OF ACTION	DAILY DOSE [MAX]	2 TIMES A WEEK DOSE [MAX]	3 TIMES A WEEK DOSE [MAX]	MAJOR ADVERSE REACTIONS*	RECOMMENDED REGULAR MONITORING	COMMENTS
Isoniazid ¹ <i>Oral or Intramuscular</i> Bactericidal	C: 5–10 mg/kg A: 5 mg/kg [300 mg]	C: 15 mg/kg A: 15 mg/kg (range 13–17 mg/kg) [900 mg]	C: 10 mg/kg A: 10 mg/kg (range 8–12 mg/kg) [900 mg]	Hepatic enzyme elevations; hepatitis; peripheral neuropathy; CNS effects; increased phenytoin levels; possible interaction with disulfiram (Antabuse®)*	Hepatic enzymes (if baseline is abnormal or patient has risk factors)	Aluminum-containing antacids reduce absorption. Pyridoxine hydrochloride (vitamin B6) may decrease peripheral neuritis and CNS effects (25 mg per day), and should be used in patients who are alcohol abusers, pregnant, breastfeeding infants, malnourished, have HIV infection, cancer, chronic renal or liver disease, diabetes, or pre-existing peripheral neuropathy.
Rifampin ¹ <i>Oral or Intravenous</i> Bactericidal	C: 10–20 mg/kg A: 600 mg (range 8–12 mg/kg) [600 mg]	C: 10–20 mg/kg A: 600 mg (range 8–12 mg/kg) [600 mg]	C: 10–20 mg/kg A: 600 mg (range 8–12 mg/kg) [600 mg]	Hepatitis; fever; thrombocytopenia; influenza-like syndrome; reduced levels of many drugs, including methadone, warfarin, hormonal forms of contraception, oral hypoglycemic agents, theophylline, dapsone, ketoconazole, PIs, and NNRTIs	Hepatic enzymes (if baseline is abnormal or patient has risk factors)	Orange discoloration of secretions, urine, tears, and contact lenses. Patients receiving methadone will need their methadone dosage increased, by an average of 50%, to avoid opioid withdrawal. Interaction with many drugs leads to decreased levels of either or both. May make glucose control more difficult in diabetics. Patients should be advised to use barrier contraceptives while on RIF. Contraindicated for patients taking most PIs and NNRTIs.
Rifabutin ² <i>Oral</i> Bactericidal	C: 10–20 mg/kg A: 5 mg/kg [300 mg]	—	—	Rash; hepatitis; fever; neutropenia; thrombocytopenia; reduced levels of many drugs, including PIs, NNRTIs, dapsone, ketoconazole, and hormonal forms of contraception	Monthly, complete blood cell count, including platelets; hepatic enzymes (if baseline is abnormal or patient has risk factors)	Orange discoloration of secretions, urine, tears, and contact lenses. Can be used daily, or in 2 or 3 times per week dosing schedule. See HIV Figure for treatment of HIV-infected persons. Adjust the daily or intermittent dose of RBT, and monitor for decreased antiretroviral activity and for RBT toxicity, if taken concurrently with PIs or NNRTIs. Contraindicated for patients taking ritonavir, saquinavir, or delavirdine. Please consult drug reference manuals for details on individual drugs. Methadone dosage generally does not need to be increased. Patients should be advised to use barrier contraceptives.
Rifapentine ³ <i>Oral</i> Bactericidal	—	—	—	Same as rifampin	Hepatic enzymes (if baseline is abnormal or patient has risk factors)	RPT should be administered once per week at a dose of 600 mg with INH 900 mg only in the continuation phase of treatment of non-cavitary drug-susceptible pulmonary TB in HIV-negative patients 12 years of age and older. Patients should be advised to use barrier contraceptives.
Pyrazinamide ¹ <i>Oral</i> Bactericidal	C: 20–30 mg/kg A: 1.5 g (≤ 50 kg) 2.0 g (51–74 kg) 2.5 g (≥ 75 kg)	C: 50 mg/kg (range 40–60 mg/kg) A: 2.5 g (≤ 50 kg) 3.0 g (51–74 kg) 3.5 g (≥ 75 kg)	C: 35 mg/kg (range 30–40 mg/kg) A: 2.0 g (≤ 50 kg) 2.5 g (51–74 kg) 3.0 g (≥ 75 kg)	Gastrointestinal (GI) upset; hepatotoxicity; hyperuricemia; gout (rarely); arthralgias; rash	Hepatic enzymes (if baseline is abnormal or patient has risk factors)	May complicate management of diabetes mellitus. Hyperuricemia can be used as indicator of compliance. Treat increased uric acid only if symptomatic.
Ethambutol <i>Oral</i> Bacteriostatic	C & A: 15–25 mg/kg [2.5 g]	C: 30–50 mg/kg A: 45 mg/kg	C: 30–50 mg/kg A: 30 mg/kg	Decreased red-green color discrimination; decreased visual acuity; skin rash	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.
Streptomycin <i>Intramuscular/ Intravenous</i> Bactericidal	C: 15–30 mg/kg A: 15 mg/kg [1000 mg]	C & A: 15 mg/kg [1000 mg]	C & A: 15 mg/kg [1000 mg]	Auditory toxicity; renal toxicity; hypokalemia; hypomagnesemia	Audiometry; renal function; electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.

Primary and Reserve Medications Notes

C = Children **A = Adults**

* All toxicities are not listed here. Full prescribing information should be checked in the package insert or pharmacology texts. Use of brand names is for informational purposes only and does not imply endorsement by the New York City Department of Health and Mental Hygiene.

1. An INH/RIF combination tablet (Rifamate®)* containing 150 mg of INH and 300 mg of RIF, and an INH/RIF/PZA combination (Rifater®)* containing 50 mg of INH, 120 mg of RIF, and 300 mg of PZA are available and should be used whenever patients are NOT on directly observed therapy.
2. Not FDA-approved for the treatment of TB.

3. RPT should not be used in HIV-infected patients.
4. Should not be used for the treatment of children, except in rare circumstances.

RESERVE MEDICATIONS USED IN THE TREATMENT OF TB: DOSAGES, MAJOR ADVERSE REACTIONS, AND RECOMMENDED REGULAR MONITORING

DRUG <i>Route of Administration</i> MODE OF ACTION	DAILY DOSE [MAX]	2 TIMES A WEEK DOSE [MAX]	3 TIMES A WEEK DOSE [MAX]	MAJOR ADVERSE REACTIONS*	RECOMMENDED REGULAR MONITORING	COMMENTS
Capreomycin <i>Intramuscular/ Intravenous</i> Bactericidal	C: 15–30 mg/kg A: 15 mg/kg [1000 mg]	—	—	Auditory, vestibular, and renal toxicity; eosinophilia; hypokalemia; hypomagnesemia	Audiometry; renal function; electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.
Ciprofloxacin ^{2,4} <i>Oral or Intravenous</i> Bacteriostatic	A: 750–1500 mg	—	—	Abdominal cramps; GI upset; tremulousness; insomnia; headache; drug interactions with warfarin and theophylline	—	Antacids containing aluminum, magnesium or calcium, and sucralfate reduce absorption and should not be given within 2 hours of the dose. The effects of caffeine may be increased. Not yet approved for use in children.
Cycloserine <i>Oral</i> Bacteriostatic	C: 15–20 mg/kg A: 500–1000 mg Divided doses	—	—	Psychosis; seizures; headache; depression; suicide; other CNS effects; rash; increased phenytoin levels	Assessment of mental status	Increase gradually, checking serum levels. Pyridoxine hydrochloride (vitamin B6) may decrease CNS effects (use 50 mg for each 250 mg of cycloserine).
Ethionamide <i>Oral</i> Bacteriostatic	C: 15–20 mg/kg A: 500–1000 mg Divided doses	—	—	GI upset; bloating; hepatotoxicity; hypothyroidism (especially with PAS); metallic taste	Hepatic enzymes (if baseline abnormal); thyroid function	Antacids/anti-emetics and lying supine for 20 minutes after dose may help tolerance. Start with 250 mg daily and increase as tolerated.
Kanamycin Amikacin ² <i>Intramuscular/ Intravenous</i> Bactericidal	C: 15–30 mg/kg A: 15 mg/kg [1000 mg]	—	—	Auditory toxicity; renal toxicity; rare vestibular toxicity; hypokalemia; hypomagnesemia	Audiometry; renal function; electrolytes	Ultrasound and warm compresses to injection site may reduce pain and induration.
Levofloxacin ^{2,4} <i>Oral or Intravenous</i> Bacteriostatic, possibly bactericidal	A: 500–1000 mg	—	—	Similar to ciprofloxacin but far fewer side effects and drug interactions	—	Similar to ciprofloxacin. Most active of the 3 fluoroquinolones commonly used for TB (ciprofloxacin, levofloxacin, ofloxacin) and is the preferred agent.
Moxifloxacin ^{2,4} <i>Oral or Intravenous</i> Bactericidal	A: 400 mg	—	—	Similar to ciprofloxacin but fewer drug interactions	—	Similar to ciprofloxacin, more active than levofloxacin against <i>M. tb</i> . There is little experience with the use of this drug for longer than 14 days. Therefore, data on adverse effects with prolonged use for TB are limited. Avoid in patients with prolonged QT interval and those receiving class Ia or III antiarrhythmic agents.
Ofloxacin ^{2,4} <i>Oral or Intravenous</i> Bacteriostatic	A: 600–800 mg	—	—	Similar to ciprofloxacin but fewer drug interactions	—	Similar to ciprofloxacin.
Para-aminosalicylic Acid <i>Oral</i> Bacteriostatic	C: 150 mg/kg A: 4 g every 12 h [12 g]	—	—	GI disturbance; hypersensitivity; hepatotoxicity; hypothyroidism; decreased digoxin levels, increased phenytoin levels; PAS levels decreased by diphenhydramine	Thyroid function	Begin gradually and increase dosage as tolerated. May cause hemolytic anemia in patients with glucose 6-phosphate dehydrogenase (G-6-PD) deficiency.

Primary and Reserve Medications Notes

C = Children A = Adults

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4. Should not be used for the treatment of children, except in rare circumstances.

Continuing Medical Education Activity Tuberculosis Treatment

SPONSORED BY THE NEW YORK CITY
DEPARTMENT OF HEALTH AND MENTAL HYGIENE

CITY HEALTH INFORMATION
VOL. 22 No.7 DECEMBER 2003

Objectives:

At the conclusion of this CME activity, participants should:

1. Be familiar with new guidelines in the treatment of TB;
2. Know the "ten basics" in the diagnosis, treatment, and prevention of TB;
3. Be familiar with dosages and major adverse reactions of anti-TB medications, and know how to monitor for adverse reactions;
4. Be able to utilize anti-TB medications in special situations such as pregnancy, TB meningitis, and renal failure;
5. Know treatment options of HIV-infected patients with TB.

Accreditation:

The continuing medical education (CME) activity is open to physicians (MDs, DOs) and physician assistants. The New York City Department of Health and Mental Hygiene is accredited by the Medical Society of the State of New York to sponsor continuing medical education for physicians. The New York City Department of Health and Mental Hygiene designates this continuing medical education activity for 2.0 hours in Category One credit toward the AMA/PRA (Physician's Recognition Award). Each physician should claim only those hours of credit that he/she actually spent on the educational activity.

Participants in CME activities sponsored by the NYC DOHMH are required to submit their name, address, and professional degree. Such information will be maintained in the Department's CME program database. If participants in CME activities so request, the information will be used by the CME Program to verify whether a professional participated in an activity and, if the activity was associated with an exam, passed the exam.

The Department will not share information in the CME database with other organizations without permission from persons included in the database, except in certain emergencies or disasters where public health agencies deem communication with all health care providers to be essential or where required by law.

Participants who provide e-mail addresses upon registration for an activity may receive electronic announcements from the Department about future CME activities as well as other public health information.

Participants must submit the accompanying exam by
June 30, 2004.

CME Activity Faculty: S Munsiff, MD, Assistant Commissioner/Director, Bureau of TB Control, NYC DOHMH; C Kambili, MD, Director of Medical Affairs (former); Bureau of TB Control, NYC DOHMH; E Barroso, MSc OM, Professional Development/CME; Bureau of TB Control, NYC DOHMH; J Burzynski, MD, MPH, Physician in Charge, Washington Heights Chest Center; Bureau of TB Control, NYC DOHMH.

CME ACTIVITY

This issue of *City Health Information*, including the continuing education activity, can be downloaded from the publications section at nyc.gov/health. To access *City Health Information* and Continuing Medical Education online, visit www.nyc.gov/html/doh/html/ch/ch.html.

INSTRUCTIONS

Read this issue of *City Health Information* for the correct answers to questions.

To receive continuing education credit, you must answer 4 of the first 5 questions correctly.

If you would like to participate in this activity by submitting the response card:

1. Complete all information on the response card, including your name, degree, mailing address, telephone number, and e-mail address. PLEASE WRITE CLEARLY.
2. Select your answers to the questions, and check the corresponding boxes on the response card.
3. Return the response card or a photocopy of the card postmarked no later than June 30, 2004.
Mail to:

CME Administrator
NYC Department of Health and Mental Hygiene
125 Worth Street, CN-29C
New York, NY 10013

QUESTIONS

1. A 39-year-old homeless man with a history of injection drug use presents to the Emergency Department with a cough of 4 weeks' duration, occasional low-grade fever, chills, night sweats, and recent weight loss. He denies prior history of TB. Chest x-ray shows an upper-lobe cavitory lesion. He is admitted to rule out TB. Which of the following is the best next step?
 A. Obtain sputum for culture and start treatment based on culture results.
 B. Obtain sputum for smear and culture, check baseline liver function tests, and immediately start anti-TB treatment.
 C. Obtain blood for liver function tests and start TB treatment only if the liver function tests are within normal limits.
 D. Obtain an HIV test and if the test is negative, wait for sputum culture results before initiating treatment because TB is unlikely in an HIV-negative individual.
2. A 3-year-old child born in New York City has risk factors for exposure to TB and was found to have a positive tuberculin skin test. The child has never traveled outside the US. He lives with his parents and maternal grandparents, who have all emigrated from Ecuador 4 years ago. The child's grandmother is currently undergoing treatment for "pneumonia" with a fluoroquinolone. Which of the following is correct?
 A. Start multidrug treatment for suspected TB regardless of chest x-ray result.
 B. Screen family members for TB only if the child's chest x-ray is abnormal.
 C. The child most likely became infected with TB from one of the adults in the household.
 D. Only report the case to the Department of Health and Mental Hygiene if cultures are positive for *Mycobacterium tuberculosis*.
3. DOT is unnecessary for:
 A. An infectious disease specialist with MDRTB
 B. The pastor of a local church with pulmonary TB
 C. A five-year-old child, both of whose parents are pediatricians
 D. None of the above
4. A 43-year-old woman is undergoing treatment with isoniazid, rifampin, pyrazinamide, and ethambutol for drug-sensitive pulmonary TB. Which of the following is NOT a contraindication for a rifampentine-based regimen in the continuation phase of treatment?
 A. A positive HIV test
 B. Sputum isolate sensitive to all TB drugs
 C. Smear-positive sputum at 8 weeks of therapy
 D. A chest x-ray with cavitory disease at the time of diagnosis
5. A 50-year-old patient is undergoing treatment for pulmonary TB with isoniazid, rifampin, pyrazinamide, and ethambutol. The culture was positive for *M. tb*. The patient returns for a visit 1 month after treatment was begun. At this time you should:
 A. Stop pyrazinamide and ethambutol and continue isoniazid and rifampin.
 B. Continue all four drugs and schedule a follow-up appointment in 2 months, since the patient tolerated the medicines well for the first month.
 C. Obtain a sputum specimen for smear and culture, continue all four drugs and see the patient in a month to review the drug-susceptibility results, assess adherence to therapy, and monitor for adverse effects.
6. How well did this continuing education activity achieve its educational objectives?
 A. Very well B. Adequately C. Poorly

CME Activity Tuberculosis Treatment

Answers

- | | | | | | | | |
|--------------------------------|-----------------------------|-----------------------------|-----------------------------|--------------------------------|-----------------------------|-----------------------------|-----------------------------|
| 1. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | D. <input type="checkbox"/> | 4. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | D. <input type="checkbox"/> |
| 2. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | D. <input type="checkbox"/> | 5. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | |
| 3. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | D. <input type="checkbox"/> | 6. A. <input type="checkbox"/> | B. <input type="checkbox"/> | C. <input type="checkbox"/> | |

Name _____

Degree _____ Telephone # _____

Address _____

E-mail address _____

Date _____

References

1. American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America. Treatment of tuberculosis. *Am J Respir Crit Care Med*. 2003;167:603–662.
2. New York City Department of Health. *Clinical Policies and Protocols*. Bureau of Tuberculosis Control. June 1999, 3rd ed. Available at: <http://www.nyc.gov/html/doh/pdf/tb/manu.pdf>. Accessed February 25, 2003.
3. New York City Department of Health and Mental Hygiene. *Antiretroviral Drugs and the Treatment of Tuberculosis*. Bureau of Tuberculosis Control. Available at: <http://www.nyc.gov/html/doh/pdf/tb/tbanti.pdf>. Accessed February 19, 2003.
4. New York City Health Code §11.03, 11.05, 11.47, 13.03, 13.05.
5. New York State Sanitary Code §2.10. Available at: <http://www.health.state.ny.us/nysdoh/epi/93/app13.pdf>. Accessed November 20, 2003.
6. New York City Department of Health and Mental Hygiene. *Tuberculosis in New York City, 2002: Information Summary*. Bureau of Tuberculosis Control. 2003. Available at: <http://www.nyc.gov/html/doh/pdf/tb/tb2002.pdf>.
7. US Department of Health & Human Services, Centers for Disease Control and Prevention (CDC). Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49:RR–6.
8. New York City Department of Health and Mental Hygiene. Testing and treatment for latent tuberculosis infection. *City Health Information*. 2000;19:1–4.

Supporting Reference

Centers for Disease Control and Prevention, American Thoracic Society. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection — United States, 2003. *MMWR* 2003;52(31):735–739.

Additional Reading

Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. *Lancet*. 2003;362:887–899.

Iseman MD. *A Clinician's Guide to Tuberculosis*. Philadelphia: Lippincott, Williams and Wilkins Publishers; 2000.

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Respondents who participate will have their responses graded immediately; participants who pass will be able to generate a certificate immediately. If participants have questions about the completion of this exam online, they may call (212) 788-5716.