CME

Treatment of Tuberculosis in Patients Infected with HIV: An Update

Target Audience: This activity is designed for physicians and nurses, and for other health care professionals who are involved in the care and support of individuals with HIV infection.

Statement of Need: The treatment of tuberculosis (TB) in the HIV-infected patient is critical and challenging for clinicians. HIV-infected patients have a 10% chance per year of developing active TB, following infection with *Mycobacterium tuberculosis* (*M. tuberculosis*). *M. tuberculosis* increases HIV replication both at local tissue sites and systemically. Studies have shown that HIV-infected patients with TB die sooner than HIV-infected patients without TB. Antiretroviral medications for HIV treatment and anti-TB regimens must be carefully staggered or coordinated to reduce interactions and toxicities, and assure effectiveness of treatment for both diseases. The U.S. Food and Drug Administration and Roche Laboratories Inc. issued a warning in February 2005 that "use of rifampin is contraindicated in HIV-infected patients receiving ritonavir-boosted saquinavir/saquinavir mesylate (Fortovase/Invirase) as part of combination antiretroviral therapy (ART) due to a high risk of hepatotoxicity." The Centers for Disease Control issued new treatment guidelines in late 2004 [*CDC. Notice to Readers: Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. MMWR 2004; 53:2*]. Clinicians treating patients with TB and/ or HIV need to know about these new guidelines for diagnosis and co-management of the two illnesses, in order to effectively treat patients. This complex dual treatment may require more intensive monitoring and involvement of medical and allied health professionals, including patient counseling and education, directly observed therapy, and case management, to increase adherence and reduce resistance to medications.

Learning Objectives: Upon the completion of this activity, participants should be able to:

- Understand the mechanism of drug interactions between the rifamycins and nonnucleoside reverse transcriptase inhibitors and protease inhibitors
- Describe the new recommendations for treatment of active TB disease in HIV-infected patients on anti-retroviral treatment
- Identify adherence-enhancing mechanisms for working with co-infected patients
- Provide the rationale for delaying anti-retroviral treatment in patients newly diagnosed with HIV infection and who have begun treatment for TB disease

Method of Instruction: Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the self-assessment test consisting of a series of multiple-choice and True/False questions.

Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a CME credit letter awarding AMA/PRA category 1 credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials.

Estimated time to complete this activity as designed is 1 hour.

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The activity was prepared in accordance with the ACCME Essentials.

This activity was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Dion Richetti, DC and Patricia Kloser, MD, MPH

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Grantor Acknowledgement: This activity is supported by an educational grant from NJDHSS Division of HIV/AIDS Services through a MOA titled, "Education and Training for Physicians and other Healthcare Professionals in the Diagnosis and Treatment of HIV/AIDS."

University of Medicine and Dentistry of New Jersey

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Division of AIDS Education

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New Jersey AIDSline

Published four times a year
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Treatment of Tuberculosis in Patients Infected with HIV: An Update

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The New Jersey Medical School National Tuberculosis Center is one of four Regional Training and Medical Consultation Centers in the United States, which are supported by a federally funded Cooperative Agreement from the Division of Tuberculosis Elimination, Centers for Disease Control and Prevention. It receives additional support through grants from the CDC, US Agency for International Development, and the NJ Department of Health and Senior Services. The Center provides training, technical assistance, and clinical consultation to health care professionals and the public through its toll-free information line (1-800-4TBDOCS), and a website with an extensive collection of downloadable materials at http://www.umdnj.edu/globaltb.

Learning Objectives:

Upon completion of this article, the reader will be able to:

- Understand the mechanisms of drug interactions between the rifamycins and nonnucleoside reverse transcriptase inhibitors and protease inhibitors
- Describe the new recommendations for treatment of active TB disease in HIV-infected patients on anti-retroviral treatment
- Identify adherence-enhancing mechanisms for working with co-infected patients
- Provide the rationale for delaying anti-retroviral treatment in patients newly diagnosed with HIV infection and who have begun treatment for TB disease

Abstract

Tuberculosis (TB) continues to be a significant risk to persons with HIV infection, as activation of latent TB infection is 100 times more likely to progress to active TB disease than in the non-HIV-infected person, and also decreases the ability to fight HIV disease progression. The CDC has updated recommendations for treatment of tuberculosis disease in HIV-infected patients, based on findings of drug interactions between the rifamycins and nonnucleoside reverse transcriptase inhibitors and protease inhibitors. Many HIV-positive patients with active TB disease should be treated for TB before antiretroviral treatment for HIV disease, to assure complete TB treatment and adherence to each complex treatment regimen. All co-infected patients should have individualized treatment including adherence-enhancing approaches such as staggering initiation of regimens, directly observed therapy, and patient counseling.

Background

The treatment of tuberculosis (TB) in the HIV-infected patient provides a challenge to the clinician. HIV-infected patients infected with Mycobacterium tuberculosis (M. tuberculosis) have a 10% chance per year of developing active TB, in contrast to the usual rate of 10% over a lifetime. HIV-infected patients have a 10% chance per year of developing active TB, following infection with *Mycobacterium tuberculosis* (*M. tuberculosis*). Studies have shown that the risk rate ratio ranges between 3.5 and 26.3 times for HIV-infected patients with positive tuberculin skin test (TST) results compared with HIV-infected patients with negative tuberculin skin test results (Table 1). *M. tuberculosis* increases HIV replication both at local tissue sites and systemically.1 Other studies have shown that HIV-infected patients with TB die sooner than HIV-infected patients without TB.2 The complexities of treatment pose additional difficulties, which require an ability to provide education and address his or her needs related to two illnesses and the management of those illnesses.

Table 1. Annual rates* of tuberculosis among persons with HIV infection, by TST status - selected years and U.S. areas

Location and source	Rate among persons with positive TST result	Rate among persons with negative TST result	Risk ratio
New York City Selwyn et al., 1989	7.9	0.3	26.3
San Francisco Daley et al., 1998	5.0	1.0	5.0
Multiple sites Markowitz et al., 1997 East Coast	4.6	1.3	3.5
West/Midwest	1.7	0.2	8.5
All sites	4.5	0.4	11.3

*Cases per 100 person-years

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TB and HIV: The Role of Immune Response

While having HIV infection is often acknowledged as contributing to many patients' development of other infections, and the impaired ability to deal with those infections, the presence of TB has a similar contribution to HIV status. Many cytokines are released as part of the host immune response to *M. tuberculosis*. Initially, alveolar macrophages encounter the tubercle bacilli and they present mycobacterial antigens to antigen specific CD4+ T-cells. These T-cells release interferon, a cytokine that activates the macrophages, and enhances their ability to control the mycobacterial infection. The activated macrophage releases pro-inflammatory cytokines, which increase HIV replication in cells. *M. tuberculosis* also increases the secretion of anti-inflammatory cytokines, which may contribute to the immune suppression often observed during TB.[3] The overall effect of *M. tuberculosis* is to accelerate the rate of progression of HIV disease.

Challenges of Treating the Co-Infected Patient: Drug-Drug Interactions

Treatment of latent TB infection with isoniazid for HIV-infected patients with positive TST results has been reported to not only decrease the incidence of TB but also to delay onset of HIV-related illnesses and to prolong survival.[4] Isoniazid poses no contraindications in the treatment of the co-infected patient on HIV-antiretroviral treatment. However, for an HIV patient who is on treatment for active TB disease, when rifamycin treatment is introduced, treatment becomes more complex, specifically, for patients on nonnucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (PI).

The principal locus of these drug-drug interactions is the cytochrome P450 (CYP) system in the intestinal wall and liver, specifically the isoenzyme CYP3A4. Rifamycins induce the activity of CYP3A4 and may substantially decrease serum concentrations of PIs and NNRTIs. Fortunately, this is not the case with the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and fusion inhibitors.

There are differences, however, between the rifamycins and their ability to induce the P450 cytochrome 3A4 oxidases. Rifampin (RIF) is the most potent inducer, rifapentene is intermediate, and rifabutin (RBT) is the least potent inducer. In addition, PIs impair the metabolism of rifamycins, resulting in increased serum levels of rifamycins, with increased risk of toxicity. With some dose adjustments, rifabutin can be safely used with most PIs and NNRTIs.

The possibility exists to treat optimally both TB and HIV disease, with rifabutin instead of rifampin, using PI or NNRTI containing HAART (Tables 2 and 3). Rifabutin has similar efficacy compared to rifampin in the treatment of TB in HIV. However, if a rifamycin is excluded from the TB treatment regimen, this may result in delayed sputum conversion, prolong the duration of therapy, and possibly result in a poorer outcome. Rifapentine, a long-acting rifamycin, is **not** recommended for the treatment of TB in HIV-infected persons because of its association with acquired rifamycin resistance.

Diagnosis of TB

There are four steps in diagnosing TB disease: medical history and examination, tuberculin skin test, chest X-ray, and bacteriologic examination. A medical history includes asking

Recommendations for Co-Administration of Rifamycins and NNRTIs and PIs

Table 2: Rifabutin (RBT)-Based Regimen

Nonnucleoside reverse transcriptase inhibitors	
RBT	NNRTI[1]
450-600 mg/day or 600 mg 3x/week 300 mg/day or 300 mg 3x/week	Efavirenz (standard dose) Nevirapine (standard dose)
Protease Inhibitors	
RBT	Single PI
150 mg/day or 300 mg 3x/week 150 mg/day or 300 mg 3x/week 150 mg/day or 300 mg 3x/week 150 mg alternate days or 3x/week 150 mg alternate days or 3x/week	Amprenavir/fos-amprenavir (usual dose) Indinavir 1000 mg TID Nelfinavir 1250 mg BID Atazanavir (usual dose) Ritonavir (usual dose)
RBT	Dual PI
150 mg alternate days or 3x/week 150 mg alternate days or 3x/week	Lopinavir/ritonavir Ritonavir (any dose) booster with saquinavir, indinavir, amprenavir, fos-amprenavir, or atazanavir
Do not use delavirdine and unboosted saquinavir with RBT	
[1]These recommendations apply to regimens that do not include PIs, which can substantially increase RBT levels.	

Table 3: Rifampin (RIF)-Based Regimen

Nonnucleoside reverse transcriptase inhibitors	
RIF	NNRTI
600 mg/day	Efavirenz 800 mg/day (max)[1]
Do not use nevirapine and delavirdine with RIF.	
Protease Inhibitors	
Do not use amprenavir, atazanvir, fos-amprenavir, indinavir, lopinavir/ritonovir, nelfinavir, ritonavir, boosted/ unboosted saquinavir, with RIF.	
[1]If efavirenz 800 mg cannot be tolerated, reduce to 600 mg.	

Source: CDC. MMWR 2004, 53:2

the patient if (s)he has been exposed to a person with TB or with symptoms of TB disease, if (s)he has had TB infection or TB disease before, or risk factors for developing TB disease. The symptoms of pulmonary TB disease may include coughing, pain in chest when breathing or coughing, coughing up sputum, and coughing up blood (hemoptysis). Systemic symptoms of TB disease (pulmonary or extrapulmonary) may include weight loss, fatigue, malaise, fever, and night sweats. The symptoms of extrapulmonary TB disease depend on the part of the body that is affected by the disease.

Patients with symptoms of TB disease should be given a Mantoux tuberculin skin test, with verification of previous skin test history, although symptomatic patients should be evaluated for TB disease immediately, regardless of their test results. Patients from countries that use the BCG vaccine often test positive, and then should be considered to have TB infection. They still need to be evaluated for active TB disease, as BCG does not prevent individuals from contracting TB, and its protective value wanes over time. The chest X-ray is used to help rule out the possibility of pulmonary TB disease in a person who has a positive reaction to the tuberculin skin test, and checks for lung abnormalities in people who have symptoms of TB disease, preferably with prior X-rays for comparison. The results, however, cannot confirm that a person has TB disease.

Finally, diagnosis of TB disease must be confirmed by bacteriologic examination, in which three sputum cultures (specimens) are obtained from patients suspected of having pulmonary TB disease; other site-specific specimens are obtained from patients suspected of having extrapulmonary TB disease; bronchoscopy may be necessary if the patient cannot cough up sputum. The specimen is examined under a microscope for the presence of acid-fast bacilli (AFB). Patients with positive smears are considered infectious, especially when AFB are numerous. The specimen is then cultured, or grown, to determine whether it contains M. tuberculosis. A positive culture for M. tuberculosis confirms the diagnosis of TB disease. After the specimen has been cultured, it is tested for drug susceptibility. The results of these tests can help clinicians choose the appropriate drugs for use in treatment.[5,6,8,11]

Beginning Antiretroviral Treatment (ART)

Often a TB patient's HIV status is unknown, and the clinician needs to counsel the patient to be tested for HIV infection. This is important for both the accurate diagnosis of TB in the patient and, subsequently, for appropriate treatment of the patient.

If a patient's HIV-positive status is discovered upon initiation of TB treatment, clinicians are required to make some decisions about the course of TB treatment and when to begin ART. In determining when to begin ART for co-infected patients, clinicians should monitor the patient's condition by measuring plasma RNA levels and CD4+ T-cell counts, and assessing the HIV-associated clinical condition to decide the timing for initiating such therapy. Together, clinicians and patients need to also consider other existing medical issues such as drug interactions and toxicities, ability to adhere to two complex treatment regimens, and laboratory abnormalities. A staggered initiation of anti-TB treatment and ART is recommended at the end of the 2-month induction phase of TB therapy or after TB therapy is completed. For some patients, switching from a RIF-based regimen to an RBT-based regimen will be necessary if ART is initiated before the completion of anti-TB treatment. However, clinicians need to plan for a 2-week "washout" period between the last dose of RIF and first doses of PIs and/or NNRTIs. Alternatively, if ART will be initiated during the anti-TB treatment, the induction phase should include RBT instead of RIF.[5,6]

All decisions should be discussed with the patient. TB treatment lasts for at least 6 months with multiple drugs. The initiation of ART adds pill burden, which can be overwhelming for the HIV-infected patient. Conversely, this is also true if the patient has already been diagnosed with HIV infection and later develops TB disease, resulting in four more drugs being added to an already complex regimen. Clinician and patient discussions should focus on how all of the patient's surrounding life circumstances may affect his or her ability to adhere to treatment along with the side effects and toxicities associated with the regimen.

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Table 4. Treatment Regimens In Patients Receiving Antiretroviral Therapy For Pansensitive Tuberculosis Organisms

<table>
<tr><th colspan="2">Induction Phase</th><th colspan="3">Continuation Phase</th></tr>
<tr><th>Drugs
Daily
mg/kg
[maximum dosage]</th><th>Duration</th><th>Drugs
Daily
mg/kg
[maximum dosage]</th><th>Drugs
3x weekly
mg/kg
[maximum dosage]</th><th>Duration</th></tr>
<tr><td>Isoniazid (INH): 5 [300][1]</td><td rowspan="5">2 months
(8 weeks)</td><td>INH: 5 [300]</td><td>INH: 15 [900]</td><td rowspan="5">4 months
(18 weeks)</td></tr>
<tr><td rowspan="4">Rifampin (RIF): 10 [600][2]
OR
Rifabutin (RBT): 5 [300][2,3]

Pyrazinamide (PZA): 20-25 [2 g]
Ethambutol (EMB): 15-20 [1.6 g]</td><td>RIF: 10 [600]</td><td>RIF: 10 [600]</td></tr>
<tr><td colspan="2">OR</td></tr>
<tr><td>INH: 5 [300]</td><td>INH: 15 [900]</td></tr>
<tr><td>RBT: 5 [300]</td><td>RBT: 5 [300]</td></tr>
</table>

[1]Pyridoxine (vitamin B6) 50 mg/day should be given to all HIV-infected patients taking INH.

[2]Rifamycins have significant interactions with methadone, oral contraceptives, and other drugs. See MMWR 2003; 52 (RR-11), p. 47.

[3]RBT dosage is based on weight and class of co-administered HIV drugs (i.e., NNRTI and/or PI) in the HAART regimen. Maximum RBT dosage varies when administered with efavirenz.

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Case Presentation: Uncovering TB and HIV

A 30-year-old Haitian man was admitted to the hospital with a history of weight loss, night sweats, high fevers, neck swelling, and diarrhea. He reported feeling well until several months prior to admission, when he noted a significant amount of weight loss, more than 30 to 40 pounds, in the last 6 months. Three to four weeks prior to admission he noted night sweats, fevers, and right-sided neck swelling. Ten to fourteen days before admission he began to experience watery diarrhea, associated with cramping and bloating.

The patient's past medical history was unremarkable. He emigrated to the United States from Haiti in 1990. He had traveled recently back to visit Haiti. He denied injection drug use, but reported numerous heterosexual sexual partners in his life. During the physical exam he was alert and in no apparent distress. Throat examination was remarkable for mild oral thrush and a neck exam revealed the right sided mass. All other exams were normal including his chest X-ray.

After various differential diagnoses were considered, a surgical biopsy was performed on the right-sided neck mass revealing pus and lymph nodes. The lymph node material revealed acid-fast bacilli, 4+ positive, and the pathology report showed necrotizing inflammation with acid fast bacilli (AFB). Three sputum specimens were collected for AFB smear and culture. **However, the patient was diagnosed as HIV positive by ELISA and Western Blot assays with a CD4+ cell count of 11 mm3 and HIV RNA was measured at 118,000 copies/ml.** The patient was started on a daily treatment regimen to cover for both *M. tuberculosis* and *M. avium* complex. The regimen consisted of: INH (300 mg), rifabutin (300 mg), PZA (1.5 g), EMB (1.2 g), and Clarithromycin (500mg BID).

How the Patient was Managed

Since the patient had been started on treatment for probable TB adenitis, the patient's physician decided to defer starting ART until the patient was on TB therapy for at least 4 to 8 weeks and wait until those medications were being well tolerated. After this phase and discussions with the patient, ART was initiated with an NNRTI (efavirenz) plus 2 NRTIs (didanosine and lamivudine), and the dosage for rifabutin was increased to 450mg. This regimen would later be modified based on final *M. tuberculosis* culture and sensitivity results.

Case Discussion: Use of the Patient-Centered Approach

As previously stated, patients suspected of having TB who have an unknown HIV-infection status should be sensitively approached about HIV testing. It is imperative that patients understand that the underlying concern is about the diagnosis and optimal treatment of TB, which makes the HIV diagnosis so important. Patients need to be educated in layperson's terminology about the immune response concerns associated with co-infection which can delay sputum conversion, making the patient's ability to feel better seem distant. It is also important that the patient understand that once he or she does feel better, the full course of anti-TB treatment still must be completed to eliminate any remaining TB bacilli.

Co-infected patients are a high priority for directly observed therapy (DOT). This means, ideally, that the ingestion of each dose of TB medication should be observed by a trained health care worker. This not only ensures adherence, but also provides a valuable link to a support system of public health outreach staff, who can monitor the patient on a regular basis for side effects as well as for unmet non-medical needs, which can affect treatment. Issues can be then immediately referred to the patient's clinician or to social services for follow up. Individualized case management is also key to the patient-centered approach. Each co-infected patient should have an assigned case manager who can monitor the patient in the clinic setting and be a "go between" for outreach and clinical staff.[7]

Summary

In conclusion, the management of TB among HIV-infected patients taking antiretroviral drugs is a challenge which can best be managed with clinician familiarity and experience with current treatment guidelines, effective patient communication, and individualized case management. This includes use of a TB treatment regimen that includes, in most cases, rifabutin instead of rifampin, a directly observed treatment regimen, and the availability of experienced and coordinated TB and HIV caregivers.

Footnotes

1. Goletti D. Weissman D. Jackson RW. Graham NM. Vlahov D. Klein RS. Munsiff SS. Ortona L. Cauda R. Fauci AS. Effect of Mycobacterium tuberculosis on HIV replication. Role of immune activation. Journal of Immunology. 157(3):1271-8, 1996 Aug 1.

2. Whalen C. Horsburgh CR. Hom D. Lahart C. Simberkoff M. Ellner J. Accelerated course of human immunodeficiency virus infection after tuberculosis. American Journal of Respiratory & Critical Care Medicine. 151(1):129-35, 1995 Jan.

3. Hirsch CS. Hussain R. Toossi Z. Dawood G. Shahid F. Ellner JJ. Cross-modulation by transforming growth factor beta in human tuberculosis: suppression of antigen-driven blastogenesis and interferon gamma production. Proceedings of the National Academy of Sciences of the United States of America. 93(8):3193-8, 1996 Apr 16.

4. Pape JW. Jean SS. Ho JL. Hafner A. Johnson WD Jr. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. Lancet. 342(8866):268-72, 1993 Jul 31.

5. CDC. Interactive Core Curriculum on Tuberculosis (2004). http://www.cdc.gov/tb/webcourses/CoreCurr/index.htm

6. CDC. Treating Opportunistic Infections Among HIV-Infected Adults and Adolescents: Recommendations of the US Public Health Service and the Infectious Diseases Society of America. MMWR 2004, 53(RR15);1-112.

7. Hoffmann-LaRoche, Inc. - Saquinavir-Rifampin Interaction [Dear Health Care Provider Letter]. New Jersey: Hoffman-La Roche; February 2005. Available at: http://www.rocheusa.com/products/invirase/Invirase_DrLetter.pdf

8. CDC. Notice to Readers: Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. MMWR 2004; 53:2

9. CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998:47.

10. CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or non-nucleoside reverse transcriptase inhibitors. MMWR 2000; 49:185-9.

11. CDC. Treatment of tuberculosis. MMWR 2003;52.

FOR MORE INFORMATION ABOUT TUBERCULOSIS AND TB-HIV CO-MANAGEMENT:

TB AND HIV CO-TREATMENT SUMMARY
from the NJ Medical School National Tuberculosis Center

- TB treatment regimens should be directly observed to assure patient adherence, and therapy should be prolonged if there is a delay in clinical or bacteriological response. The continuation phase should be extended from 4 to 7 months (9 months of total treatment) if the 2-month treatment culture is positive and if there is cavitation indicated by a chest x-ray at 4 months of treatment.
- Although the principles of TB treatment are similar for children and adults, unique considerations must be followed when treating HIV and TB co-infected children. Children should be treated without delay. However, consultation with a specialist who has experience managing co-infected children is advised because indications for antiretroviral therapy, dosing of medications, and optimal length of therapy in children can vary.
- To prevent acquired rifamycin resistance in persons with advanced HIV infection (CD4+ cell counts ‹100/µl) and TB, use more frequent therapy (3x weekly or daily) with RIF or RBT-based therapies.
- Rifapentine, a long-acting rifamycin, is not recommended for the treatment of TB in HIV-infected persons because of its association with acquired rifamycin resistance.

As HIV and TB treatment guidelines change frequently, consult http://www.cdc.gov/tb and http://aidsinfo.nih.gov for up-to-date information, in addition to the references listed below.

Tuberculosis in New Jersey

Tuberculosis Is a reportable disease: physicians, advanced practice nurses, physicians' assistants, persons having control or supervision over a health care facility, school, summer camp, childcare center, preschool, or institution of higher education are required to report a suspected or confirmed tuberculosis diagnosis within 24 hours. TB suspected or confirmed cases are reportable directly to the New Jersey Department of Health and Senior Services, TB Program at 609-588-7522.

TB in NJ is declining but still a concern, especially for people with HIV: from calendar year (CY) 1992 to CY2004 newly reported TB cases declined by 51.0 percent (984 to 482) cases annually. A similar reduction in is reported for Active TB cases Co-infected with HIV, New Jersey, 1993-2004, from 239 in 1993 to 44 in 2004. It is important to note that while the 482 cases reported in CY2004 represent a new historical annual low in New Jersey, continued vigilance is needed through initiation of expert case management and the use of Directly Observed Therapy (DOT) to continue this downward trend. For more information about the New Jersey Tuberculosis Program: http://www.state.nj.us/health/cd/tbhome.htm

Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination (DTBE)

www.cdc.gov/tb

- CDC. New CDC Program for Rapid Genotyping of Mycobacterium tuberculosis Isolates. MMWR 2005:54: 47.
- CDC. Treating Opportunistic Infections Among HIV-Infected Adults and Adolescents Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America MMWR:2004; 53, No. RR15;1-112. http://www.cdc.gov/mmwr/PDF/RR/RR5315.pdf
- CDC. Treatment of tuberculosis. MMWR 2003; 52 (RR-11).
- CDC. Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. MMWR 2004; 53:37.
- Interactive Core Curriculum on Tuberculosis [2004]

  http://www.cdc.gov/tb/webcourses/CoreCurr/index.htm

  This on-line course includes chapters on:

  1) Tuberculosis in the United States
  2) Transmission and Pathogenesis of Tuberculosis
  3) Testing for Tuberculosis Disease and Infection
  4) Diagnosis of Tuberculosis
  5) Treatment of Latent Tuberculosis Infection
  6) Treatment of Tuberculosis Disease
  7) Infection Control in Health Care Settings
  8) BCG Vaccination
  9) Community Tuberculosis Control.

  On average, it takes approximately 5 hours to complete the entire 9-chapter course. The CDC provides free on-line continuing education credit for physicians, nurses, and health educators. TB recommendations change often.
- Consult the CDC Tuberculosis website for updates to recommendations: www.cdc.gov/tb.

American Academy of Pediatrics, Committee on Infectious Diseases. Tuberculosis. In L.K. Pickering (Ed.), 2003 Red Book: Report of the Committee on Infectious Diseases. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2003:642-660.

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CME QUIZ

Treatment of Tuberculosis in Patients Infected with HIV: An Update

Questions refer to the content of the article and the notes that follow. To receive CME credit: complete exam, registration, and evaluation forms on-line at http://ccoe.umdnj.edu/aids or fill in the forms on the next 2 pages, and mail or fax to UMDNJ-CCOE (see next page).

1. Which of the following anti-TB drugs has the greatest ability to decrease serum levels of certain HIV anti-retroviral drugs?

   a. Rifampin
   b. Ribabutin
   c. Isoniazid
   d. Rifapentine

2. Rifampin can be safely used with boosted saquinavir.

   a. True
   b. False

3. For which category of antiretroviral therapy do rifamycins induce the P450 cytochrome 3A4 oxidases?

   a. Nucleoside reverse transcriptase inhibitors
   b. Non-nucleoside reverse transcriptase inhibitors
   c. Fusion inhibitors
   d. Nucleotide reverse transcriptase inhibitors

4. In determining when to begin anti-retroviral therapy in a TB and HIV co-infected patient who is on four-drug anti-TB treatment, the following factors should be taken into consideration:

   a. The patient's ability to adhere to the TB and HIV treatment regimens
   b. The patient's CD4+ T-cell counts
   c. Laboratory abnormalities
   d. All of the above

5. For patients switching from a RIF-based regimen to an RBT-based regimen, in order to initiate anti-retroviral therapy, how long is the "washout" period between the last dose of RIF and first doses of PIs and/or NNRTIs?

   a. 1 week
   b. 2 weeks
   c. 3 weeks
   d. 4 weeks

6. What dose of pyridoxine should be given to HIV-infected patients taking INH?

   a. 25 mg
   b. 50 mg
   c. 75 mg
   d. 100 mg

7. Which is the following is NOT part of the patient-centered approach to working with TB and HIV co-infected patients?

   a. Case management
   b. Directly observed therapy
   c. Patient education
   d. Self-administration of TB medications

8. The only HIV drug which is recommended for use with rifampin is:

   a. Nevirapine
   b. Saquinavir + ritonavir
   c. Efavirenz
   d. Lopinavir/ritonavir

9. When would it be prudent to add "coverage" for atypical tuberculosis in an HIV-positive patient whose smear is positive for AFB?

   a. The patient is on Kaletra
   b. The CD4+ count is more than 250
   c. The patient has a CD4+ count under 50 and extrapulmonary AFB
   d. The patient has severe weight loss

10. What are the advantages of DOT?

a. Ensure adherence to medication

   b. Provide opportunities to educate patient about TB and medication side effects
   c. Enable healthcare worker to educate patient about HIV and HIV testing
   d. All of the above

University of Medicine and Dentistry of New Jersey
Center for Continuing and Outreach Education

Treatment of Tuberculosis In Patients Infected with HIV: An Update

Registration Form

In order to obtain AMA PRA category 1 credit, participants are required to:

(1) Read the learning objectives, and review the activity, and complete the self-assessment.

(2) Complete this registration form and the activity evaluation form on the reverse side, and record your test answers below

(3) Send the registration and evaluation forms to:

UMDNJ-Center for Continuing and Outreach Education

via mail: PO Box 1709, Newark, NJ 07101-1709

via fax: (973) 972-7128

(4) Retain a copy of your test answers. Your answer sheet will be graded and if a passing score of 70% or more is achieved, a CME credit letter awarding AMA/PRA category 1 credit and the test answer key will be mailed to you within four (4) weeks. Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again.

Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again. This activity will be posted online at http://ccoe.umdnj.edu/aids

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

SELF-ASSESSMENT TEST

Circle the best answer for each question on page 10.

1. A B C D
2. A B
3. A B C D
4. A B C D
5. A B C D
6. A B C D
7. A B C D
8. A B C D
9. A B C D
10. A B C D

Registration

First Name_____M.I._____ Last Name_____Degree_____

Social Security #_____(for credit recording purposes only)

Daytime Phone # _____ Evening Phone #_____

Fax #_____ E-mail_____

Preferred Mailing Address: Home Business

Address_____

City_____State_____Zip Code_____

Affiliation, Specialty_____

I attest that I have completed the activity as designed and I am claiming [up to 1 credit] _____ AMA/PRA category 1 credit

Signature_____ Date_____

Credit for this activity is available until December 31, 2006
UMDNJ-Center for Continuing and Outreach Education
PO Box 1709, Newark, NJ 07101-1709
Phone: 973-972-4267 or 1-800-227-4852

CE Activity Code: 07HC06-DE0

CME

University of Medicine and Dentistry of New Jersey
Center for Continuing and Outreach Education

Treatment of Tuberculosis in Patients Infected with HIV: An Update

Activity Evaluation Form

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants. Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of this completed evaluation form. Thank you for your cooperation!

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:	Strongly Agree				Strongly Disagree
Objective 1: Understand the mechanism of drug interactions between the rifamycins and nonnucleoside reverse transcriptase inhibitors and protease inhibitors.	5	4	3	2	1
Objective 2: Describe the new recommendations for treatment of active TB disease in HIV-infected patients on anti-retroviral treatment.	5	4	3	2	1
Objective 3: Identify adherence-enhancing mechanisms for working with co-infected patients.	5	4	3	2	1
Objective 4: Provide the rationale for delaying anti-retroviral treatment in patients newly diagnosed with HIV-infection and who have begun treatment for TB disease.	**5**	**4**	**3**	**2**	**1**

OVERALL EVALUATION:	Strongly Agree				Strongly Disagree
The information presented increased my awareness/understanding of the subject.	5	4	3	2	1
The information presented will influence how I practice.	5	4	3	2	1
The information presented will help me improve patient care.	5	4	3	2	1
The faculty demonstrated current knowledge of the subject.	5	4	3	2	1
The program was educationally sound and scientifically balanced.	5	4	3	2	1
The program avoided commercial bias or influence.	5	4	3	2	1
Overall, the program met my expectations.	5	4	3	2	1
I would recommend this program to my colleagues.	5	4	3	2	1

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

_____

_____

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Please provide any additional comments pertaining to this activity (positives and negatives) and suggestions for improvement:

Please list any topics that you would like to be addressed in future educational activities:

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_____

CE Activity Code: 07HC06-DE01