



HEPP NEWS

March 2001 Vol. 4, Issue 3

HIV
EDUCATION
PRISON
PROJECT

Sponsored by the Brown Medical School Office of Continuing Medical Education and the Brown University AIDS Program.

ABOUT HEPP

HEPP News, a forum for correctional problem solving, targets correctional administrators and HIV/AIDS care providers including physicians, nurses, outreach workers, and case managers. Published monthly and distributed by fax, HEPP News provides up-to-the-moment information on HIV treatment, efficient approaches to administering HIV treatment in the correctional environment, national and international news related to HIV in prisons and jails, and changes in correctional care that impact HIV treatment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education to physicians who accurately respond to the questions on the last page of the newsletter.

EDITORS

Anne S. De Groot, M.D.
Director, TB/HIV Research Lab,
Brown Medical School

Frederick L. Altice, M.D.
Director, HIV in Prisons Program,
Yale University AIDS Program

Joseph Bick, M.D.
Director, HIV Treatment Services,
California Medical Facility,
California Department of Corrections

FACULTY DISCLOSURE

In accordance with the Accreditation Council for Continuing Medical Education Standards for Commercial Support, the faculty for this activity have been asked to complete Conflict of Interest Disclosure forms. Disclosures are listed at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV unless otherwise indicated. For the treatment of HIV infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

HEPP News is grateful for the support of Abbott Laboratories, Agouron Pharmaceuticals, Boehringer-Ingelheim/Roxane Laboratories, Dupont, Merck & Co. and Roche Pharmaceuticals through unrestricted educational grants.

TB AND THE HIV-POSITIVE PRISONER

Rachel Maddow^{*^}, Andrew Vernon, MD, MHS^{**^}, Carol J. Pozsik, RN, MPH^{***^}

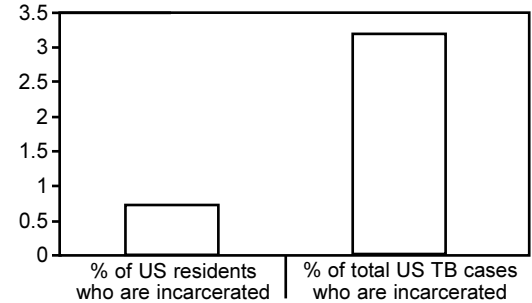
There is a perilous synergy between HIV and tuberculosis in correctional facilities. Prisoners, who have long been known to have disproportionately high rates of diagnosed TB disease and TB infection,¹ (See Figure 1) also have more than 5 times the general population's rate of AIDS, and between 4 and 10 times the general population's rate of HIV infection.² Crowding, poor ventilation, the high prevalence of HIV among prisoners, and the higher prevalence of TB in the communities from which prisoners are disproportionately drawn can make correctional facilities key sites of amplification for TB transmission. This article will review the interactions between HIV and TB in correctional settings, describe a recent outbreak of TB in a facility where HIV-infected inmates are segregated, and address the treatment of TB in HIV-infected individuals.

THE BROAD RIVER OUTBREAK

During the Spring of 2000, South Carolina reported a significant TB outbreak among HIV-positive prisoners.³ Contemporaneously, the Institute of Medicine released a report on the lamentable state of TB eradication,⁴ and the CDC released updated guidelines for simultaneous treatment of HIV and TB⁵ and new guidance on targeted screening and treatment of latent TB infection.⁶ The South Carolina outbreak serves as a compelling reminder that this emphasis on guidelines and standards for TB in prisons and jails is well justified.

In August 1999, two men who had been housed on the HIV-segregation unit in the Broad River Men's Correctional Institution in Columbia, South Carolina were diagnosed with sputum smear-positive pulmonary tuberculosis.⁷ The first patient had a previously documented tuberculin skin test reaction of 15 mm in 1984 and two subsequent incomplete attempts at isoniazid prophylaxis. Six weeks before his TB diagnosis, in July 1999, he was admitted to a community hospital with fever, abdominal pain, and cough. The patient's chest radiograph was normal and, despite existing guidelines for the treatment of HIV-infected, PPD positive individuals (See HEPP News March 2000, and Prevention and Treatment of Tuberculosis Among Patients Infected with Human Immunodeficiency Virus: Principles of Therapy

FIGURE 1. Prisoners among US TB cases and US residents, 1999. In 1999, prisoners made up 0.73% of US residents, but they made up 3.3% of all US TB cases.



and Revised Recommendations, MMWR 1998; 47(No. RR-20):1-58), no sputum specimens were obtained for AFB smear and culture. He was not placed in respiratory isolation and was returned to the prison. Six weeks later, in mid-August, the patient returned to the community hospital, where he was diagnosed with active TB. Later that month, South Carolina Department of Corrections (DOC) staff learned that another prisoner who had been released from the same HIV-segregation unit in July 1999 had been diagnosed with active TB.⁸

The SC DOC and the state's Department of Health and Environmental Control initiated a contact investigation, and invited collaboration from the Centers for Disease Control and Prevention. Contact investigators tracked down current prisoners who had come into contact with the source case-patient (he had participated in congregate religious activity, including bible study),⁹ as well as more than 100 prisoners who had lived in the source-case patient's dormitory but had since been released into the community. By the time CDC reported on the investigation in November 2000,¹⁰ over 320 current or former inmates from the HIV-segregation unit were found to have been exposed to MTB and 31 were diagnosed with TB disease.

Continued on page 2

WHAT'S INSIDE

Ask the Expert	pg 5
HEPPigram	pg 6
HIV101.....	pg 7
Self-Assessment Test	pg 9

TB AND THE HIV-POSITIVE PRISONER...

(continued from page 1)

In addition, a medical student who had examined the initial source case-patient in the community hospital in July developed cavitory TB. Notably, IS6110-based DNA fingerprints of all 20 available outbreak-associated *M. tuberculosis* isolates were identical.¹¹

REPEATING HISTORY

Although the South Carolina outbreak was due to a drug-susceptible strain of TB, it was a reminder of the deadly 1990-1991 outbreak of multi-drug-resistant TB in New York prisons and jails.¹² Of the 39 New York inmates identified with MDR-TB, 38 were HIV-positive.¹³ As an airborne infection, TB presents one of the most immediate health threats not only to prisoners, but also to correctional staff, health care providers, visitors, and others who come in close contact with TB patients.

The single most potent factor affecting the risk of progression from latent TB infection to active TB disease is HIV coinfection.¹⁴ It is often more difficult to detect active TB in persons with HIV/AIDS because they may not respond to the tuberculin skin test, and they may present atypical or negative findings on chest x-ray.¹⁵ Furthermore, significant drug interactions may complicate the concurrent treatment of HIV and TB.¹⁶ In short, HIV increases the risk of progression from TB infection to disease, makes screening for TB more difficult, and complicates the treatment of TB. (Refer to HEPPigram on page 6.)

For New York State, the 1990-1991 outbreak was a catalyst for overhauling the DOC's anti-TB efforts. TB protocols were modified to reflect heightened levels of scrutiny for HIV-infected individuals who might be harboring TB. Stepped-up monitoring and treatment resulted in a 73% decrease in the NYDOC's TB incidence rate (per 100,000 population) from 225 in 1991 to 61 in 1997.¹⁷

THINK TB! SCREENING AND TREATING PRISONERS

As recommended by the National Commission for Correctional Health Care, all prisoners should receive tuberculosis symptom screening on intake; anyone with TB symptoms (chronic productive cough, fever, weight loss, night sweats) should immediately be moved to a negative pressure respiratory isolation room and evaluated for TB disease. Tuberculin skin tests (TST) should be administered to all prisoners who have not had a previous documented positive skin test result. A TST reaction (induration at 48-72 hours) of greater than 10mm should be taken as indicative of TB infection in HIV-negative prisoners; however, in HIV-infected individ-

TABLE 1. Treating Latent TB Infection in HIV-Positive Patients*

DRUG	REGIMEN	DOSAGE	CRITERIA FOR COMPLETION
INH isoniazid	Daily for 9 months	5 mg/kg (adults) up to 300 mg	= 270 doses w/in 12 mos
INH isoniazid	2 x / week for 9 mos	15 mg/kg (adults) up to 900 mg	= 76 doses w/in 12 mos DOT MUST BE USED**
RIF rifampin + PZA pyrazinamide	Daily for 2 months	RIF 10 mg/kg (adults) (600mg) PZA 15-20 mg/kg (adults) (2g)	Alternate regimen for HIV+ (and HIV-) adults DOT MUST BE USED**

*adapted from the New Jersey Medical School National TB Center (NTBC) pocket guide. To obtain call 973-972-3270.

** DOT is always preferred in prison and jail settings. With 2x weekly dosings DOT must be used.

uals and in recent contacts of an active case, the threshold is only 5mm. Any patient whose TST indicates TB infection, and all HIV-positive patients, should receive a chest x-ray. It should be noted that TST may fail to identify TB infection in high-risk patients including prisoners.¹⁸ TB control officers may consider using on-site chest radiography to screen all prisoners at entry (see HEPP News March 2000). HIV-positive patients with TB may be unresponsive to TST¹⁹ - and even chest x-rays may fail to demonstrate abnormalities in HIV-positive patients with TB disease. It is therefore recommended that any HIV-positive patient with respiratory symptoms undergo a sputum analysis in addition to a chest x-ray.

Prisoners with documented latent TB infection (LTBI) should complete a course of treatment.²⁰ Several regimens are currently recommended; for HIV-positive patients not taking HAART, guidelines for treating latent TB infection are substantially similar to those for persons who are HIV-negative (see Table 1).

Those with a positive TST who cannot complete treatment for latent TB infection (LTBI) should receive regular screening for TB symptoms (South Carolina's TB Control Division recommends quarterly screening); any such patient with significant immune suppression should be scrutinized for TB symptoms even more frequently. Prisoners who clear the initial TB intake screening should be evaluated at least yearly for TST conversion, and more frequently if there is evidence of recent transmission of TB in the facility or if prisoners with HIV are housed together.²¹

TREATING ACTIVE TB IN THE HIV-POSITIVE PATIENT

HIV-positive persons with active TB are always candidates for HAART (if not already on HAART) since active TB infection is itself an AIDS-defining illness. While it may sometimes be feasible to delay HAART treatment in order to start treatment for TB disease, the converse is not

true: there is no clinical justification for delaying the treatment of active TB.

The complicated nature of coadministering treatment for active TB and HAART is due to the fact that the rifamycin drugs used to treat TB (usually rifampin or rifabutin) stimulate the same liver enzyme systems (CYP450) that process protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs).²² Non-rifamycin TB drugs (such as isoniazid) do not generally interact with HAART medications. However, treatment of active TB in HIV-positive persons using regimens lacking a rifamycin is regarded as sub-optimal and is not recommended.²³ CDC guidelines for the concurrent treatment of HIV and TB were updated in March 2000.²⁴ Previous guidelines had advised that rifampin not be administered to an HIV-positive patient taking any PI or NNRTI, but the update advises that rifampin can probably be co-administered with these three HAART regimens: (1) when HAART includes the NNRTI efavirenz and two NRTIs, (2) when HAART includes ritonavir and one or more NRTIs, and (3) when HAART includes a combination of ritonavir and saquinavir (either hard gel or soft gel).

(Data were also presented at the 8th Retroviruses Conference in Chicago in February suggesting that it may be necessary to increase efavirenz dosage to 800 mg/qd when used in combination with rifampin. See HIV 101, page 7 for a complete chart of dosages).²⁵

In addition, the CDC had previously recommended that rifabutin could safely be used with any PI other than ritonavir and any NNRTI other than delavirdine. The new recommendations advise that rifabutin may be co-administered with ritonavir (with or without saquinavir), but that the dosage of rifabutin should be reduced substantially to 150 mg two or three times per week. While there are not substantial clinical data on the subject, the CDC recommends that it is possible to administer rifabutin with the PIs

Continued on page 4

LETTER FROM THE EDITOR

Dear Colleagues,

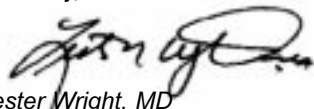
HIV infection is relatively difficult to acquire, but its frequent co-infection, TB, is acquired by the simple act of breathing. And, when we are doing our breathing in a congregate setting, such as a prison or jail, we and our families can be at risk. That is why aggressive TB control in corrections is critically important not only to corrections but also to our communities.

New York State Department of Correctional Services (NYSDOCS) conducts a TB skin test on everyone in our system at least every year, and has a high index of suspicion for TB. Approximately 25% of the inmates we receive have TB infection. We require that any time sputum testing for AFB is done, it must take place in negative pressure and the patient must be isolated at least until three negative smear results are available (or until cultures have returned if the patient has symptoms). Thus we have a presumption of TB until proven otherwise. At the NYSDOCS, we believe that in our setting, and with our history as a system, if we are concerned enough to get sputums for AFB we should be concerned enough to isolate until we know the results. The majority of our inmates come from New York City and many have risk factors for developing TB disease. In the 10 years that we have been taking TB so seriously we have seen incidence of TB disease in our system decrease from 225/100,000 to 26/100,000. This is approximately the TB incidence rate of Manhattan! Since we give all TB medications, both for treatment and for prophylaxis, by directly observed therapy, we have seen a major decrease in MDR disease; with only one case in the last two years.

HIV 101 this month covers interactions between antiretrovirals and rifamycins. The HEPPigram is an algorithm for managing a positive PPD skin test on routine screening. In our "Ask the Expert" piece, Dr. Jane Carter of Rhode Island discusses a case of active tuberculosis in a patient recently diagnosed with HIV. After reviewing this issue, readers should be able to describe the best management for TB cases in corrections, choose a suitable regimen for co-administering HIV and TB medications, and list some of the challenges presented in the treatment of co-infection.

Next month we'll bring you the latest on Hepatitis C treatment and management. Feel free to write us with questions or suggestions on how we can be a better resource!

Sincerely,



Lester Wright, MD

Senior Advisors

Theodore M. Hammett, Ph.D.
Abt Associates

Ned E. Heltzer, R.Ph., M.S.
Prison Health Services, Inc.

Ralf Jürgens
Canadian AIDS Law Legal Network

David P. Paar, M.D.
University of Texas Medical Branch

Joseph Paris, Ph.D., M.D.
CCHP Georgia Dept. of Corrections

Khurram Rana, Pharm. D.
University of RI College of Pharmacy

David Thomas, J.D., M.D.
Florida Dept. of Corrections

Lester Wright, M.D.
New York State Dept. of Corrections

Associate Editors

Anne C. Spaulding, M.D.
Brown Medical School

Stephen Tabet, M.D., M.P.H.
Univ. of Washington Division of Infectious Disease Seattle HIVNET

David A. Wohl, M.D.
University of North Carolina

Managers

Dennis Thomas
Brown University AIDS Program

Michelle Gaseau
The Corrections Connection

Layout

Kimberly Backlund-Lewis
The Corrections Connection

Distribution

Screened Images Multimedia

Managing Editor

Elizabeth Stubblefield
HIV Education Prison Project

Contributing Writer

Rachel Maddow
HIV Education Prison Project

The editorial board and contributors to HEPP News include national and regional correctional professionals, selected on the basis of their experience with HIV care in the correctional setting and their familiarity with current HIV treatment. We encourage submissions, feedback, and correspondence from our readership.

SUBSCRIBE TO HEPP NEWS

Fax to 617.770.3339 for any of the following: (please print clearly or type)

- Yes, I would like to add/update/correct (circle one) my contact information for my complimentary subscription of HEPP News fax/email newsletter.
- Yes, I would like to sign up the following colleague to receive a complimentary subscription of HEPP News fax/email newsletter.
- Yes, I would like to have the following back issues emailed to me (please include volume/issue/date).
- Yes, I would like my HEPP News to be delivered in the future as an attached PDF file in an email (rather than have a fax).

NAME: _____

FACILITY: _____ (Optional) # of HIV-Infected Inmates: _____

CHECK ONE: Physician Physician Assistant Nurse Practitioner Nurse/Nurse Administrator
 Pharmacist Medical Director/Administrator HIV Case Worker/Counselor Other

ADDRESS: _____

CITY: _____ STATE: _____ ZIP: _____

FAX: _____ PHONE: _____ EMAIL: _____

SIGNATURE: _____ DATE: _____

TB AND THE HIV-POSITIVE PRISONER...

(continued from page 2)

saquinavir, nelfinavir, or amprenavir and the NNRTI nevirapine without reducing the dosage of rifabutin. Rifabutin should not be used with the NNRTI delavirdine. When rifabutin is used concurrently with the NNRTI efavirenz, the dosage of rifabutin should be increased (to either 450 mg or 600 mg daily or 600 mg two or three times per week).

The exact appropriate dosages of the rifamycins (either rifampin or rifabutin) may vary depending on the exact HAART medications and dosages (See HIV 101, page 7). In HAART regimens that contain multiple PIs or PI/NNRTI combinations, there is little clinical experience and no firm guidance from CDC; state health authorities and experts in HIV/TB coinfection should be consulted. Updated guidelines and information on TB diagnosis and treatment can always be found on the CDC's Division of TB Elimination website: <http://www.cdc.gov/nchstp/tb>.

OTHER DRUG CAUTIONS FOR TB TREATMENT

It should also be noted that two non-HAART drugs commonly administered to HIV-positive patients, fluconazole and clarithromycin, both cause an increase in rifabutin levels. Both fluconazole and clarithromycin cause this effect independently, and the effect is more-than-doubled when both are present. Clinicians should monitor for rifabutin toxicity (arthralgia, neutropenia, uveitis) when co-administering fluconazole and/or clarithromycin.²⁶

Any patient taking isoniazid or pyrazinamide should be cautioned about hepatotoxicity and monitored for its symptoms, which can include nausea, vomiting, jaundice, abdominal pain, and anorexia. The risk of hepatotoxicity is probably greater in persons with acute hepatitis, chronic liver disease, injecting drug use history, prior intolerance of either medication, chronic alcoholism, or current use of interacting medications. Correctional clinicians should obtain baseline hepatic measurements of serum AST (SGOT) or ALT (SGPT) and bilirubin before starting therapy for TB infection, and may need to consider more frequent monitoring of

clinical and/or biochemical status when either medication is used in treating latent TB infection. A forthcoming report (MMWR, April 2001) from the CDC will give additional data on serious adverse reactions associated with treatment for latent TB infection. Adverse reactions to a two month regimen of rifampin and pyrazinamide can be serious or even fatal, and patients should be monitored closely for liver toxicity. For additional information on optimal monitoring approaches, providers may wish to access information provided at the National TB Center TB Infoline 1-800-4TB DOCS or <http://www.umdj.edu/ntbc>.

CONCLUSION

Two maxims are critical to TB control in correctional settings: "Think TB!" and "Consult an expert". TB specialists are available through the departments of public health in every state, and CDC experts are available for additional consultation. All it takes to transmit TB is to share airspace with an active TB case. Correctional providers and staff are also at risk when active TB is present in a prison or jail setting.

*HEPP News Staff Writer

**Supervisory Medical Epidemiologist, Research and Evaluation Branch, Project Officer, TB Trials Consortium, Division of TB Elimination, NCHSTP, CDC

***Director, TB Control Division, SC Department of Health and Environmental Control

[^]Nothing to disclose.

REFERENCES:

- 1.CDC. Prevention and control of tuberculosis in correctional facilities: recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1996; 45(No. RR-8):2.
- 2.Hammitt, TM; Rhodes, W; Harmon P 'HIV/AIDS and Other Infectious Diseases Among Correctional Inmates: A Public Health Problem and Opportunity' National HIV Prevention Conference 1999. Atlanta, GA. Abstract 571.
- 3.CDC. Drug-susceptible Tuberculosis Outbreak in a State Correctional Facility Housing HIV-Infected Inmates - South Carolina, 1999-2000. *MMWR* 2000; 49(46):1041-4. Spradling P, McLaughlin S, Drociuk D, et al 'Transmission of mycobacterium tuberculosis among inmates in an HIV-dedicated prison dormitory' XIII International AIDS Conference 2000. Durban, South Africa. Abstract ThPeB5188.
- 4.Institute of Medicine. Ending Neglect: The Elimination of Tuberculosis in the United States. Washington, DC: National Academy Press. 2000.
- 5.CDC. Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nucleoside Reverse Transcriptase Inhibitors. *MMWR* 2000; 49(09):185-9.
- 6.CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000; 49(No. RR-6):1-51.
- 7.American Health Consultants 'TB plus HIV cause big trouble for prison, jail in two Southern states' *TB Monitor* 2000; 7(8):77-79.
- 8.CDC. Drug-susceptible Tuberculosis Outbreak in a State Correctional Facility Housing HIV-Infected Inmates - South Carolina, 1999-2000. *MMWR* 2000; 49(46):1041-4.
- 9.American Health Consultants 'TB plus HIV cause big trouble for prison, jail in two Southern states' *TB Monitor* 2000; 7(8):77-79.
- 10.CDC. Drug-susceptible Tuberculosis Outbreak in a State Correctional Facility Housing HIV-Infected Inmates - South Carolina, 1999-2000. *MMWR* 2000; 49(46):1041-4.
- 11.CDC. Drug-susceptible Tuberculosis Outbreak in a State Correctional Facility Housing HIV-Infected Inmates - South Carolina, 1999-2000. *MMWR* 2000; 49(46):1041-4.
- 12.CDC. Transmission of Multidrug-Resistant Tuberculosis Among Immunocompromised Persons in a Correctional System - New York, 1991. *MMWR* 1992; 41(28):507-9.
- 13.Valway SE, Greiffinger RB, Papania M, et al 'Multidrug-resistant tuberculosis in the New York State prison system, 1990-1991' *J Infect Dis* 1994 Jul; 170(1):151-6.
- 14.CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000; 49(No. RR-6):8
- 15.CDC. Drug-susceptible Tuberculosis Outbreak in a State Correctional Facility Housing HIV-Infected Inmates - South Carolina, 1999-2000. *MMWR* 2000; 49(46):1041-4.
- 16.Burman WJ, Galliciano K, Peloquin C 'Therapeutic implications of drug interactions in the treatment of human immunodeficiency virus-related tuberculosis' *Clin Infect Dis* 1999 Mar; 28(3):419-29.
- 17.Klopf LC 'Tuberculosis control in the New York State Department of Correctional Services: a case management approach' *Am J Infect Control* 1998 Oct; 26(5):534-7.
- 18.Zoloth SR, Safyer S, Rosen J, et al 'Anergy compromises screening for tuberculosis in high-risk populations' *Am J Public Health* 1993 May; 83(5):749-51.
- 19.Periman DC, el-Sadr WM, Nelson ET, et al. Variations of chest radiographic patterns in pulmonary tuberculosis by degree of human immunodeficiency virus-related immunosuppression: Terry Bein Community Programs for Clinical Research on AIDS (CPCRA). *Clin Infect Dis* 1997; 25:242-6.
- 20.CDC. Prevention and control of tuberculosis in correctional facilities: recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1996;45(No. RR-8):1-28. CDC. Prevention and Treatment of Tuberculosis Among Patients Infected with Human Immunodeficiency Virus: Principles of Therapy and Revised Recommendations. *MMWR* 1998; 47(No. RR-20):1-58.
- 21.CDC. Prevention and control of tuberculosis in correctional facilities: recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1996;45(No. RR-8):1-28.
- 22.Munsiff SS, Fujiwara PI 'Treatment of Tuberculosis in Patients Taking Antiretrovirals' *AIDS Reader* 2000; 10(2):102-108.
- 23.CDC. Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nucleoside Reverse Transcriptase Inhibitors. *MMWR* 2000; 49(09):185-9.
- 24.CDC. Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nucleoside Reverse Transcriptase Inhibitors. *MMWR* 2000; 49(09):185-9.
- 25.Lopez-Cortes LF, Ruiz R, Viciano P, et al 'Pharmacokinetic Interactions between Rifampin and Efavirenz in Patients with Tuberculosis and HIV Infection' 8th Conference on Retroviruses and Opportunistic Infections 2001. Chicago, IL. Abstract 32.
- 26.Jordan MK, Polis MA, Kelly G, et al 'Effects of fluconazole and clarithromycin on rifabutin and 25-O-desacetyl-rifabutin pharmacokinetics' *Antimicrob Agents Chemother* 2000; 44(8):2170-2.

ASK THE EXPERT: Double Trouble in Guantanamo Bay

by Jane Carter, M.D.**Clinical Assistant Professor of Medicine, Division of Infectious Disease, Pulmonary and Critical Care, Brown University Medical Director, TB Clinic of Rhode Island*

CASE:

A 46-year-old Haitian gentleman presented to the general medical clinic at Guantanamo Bay for evaluation of fevers. He speaks only Haitian Creole. He denies all localizing symptoms, specifically headache, cough, sputum production, dysuria, diarrhea or myalgias. Chest radiography (CXR), blood work, and cultures are normal. A diagnosis of viral syndrome was made.

Two weeks later he returns continuing to complain of fever. Physical examination reveals a temperature of 105.5 degrees and enlarged right cervical lymph node. His CXR is repeated, demonstrating a faint left upper lobe infiltrate that was, in retrospect, present on the previous film.

He is admitted to the hospital and started on broad spectrum antibiotics for outpatient acquired pneumonia. Sputum samples were obtained, he was 3+AFB smear positive. He was started on Isoniazid (INH), Rifampin, Pyrazinamide (PZA), Ethambutol and Capreomycin.

Drug susceptibility testing for his TB isolate returned demonstrating a fully susceptible organism. Capreomycin and Ethambutol were discontinued. On TB treatment, his lymph nodes regressed in size. Fevers disappeared. His sputum reverted to smear negative. After he was noted to have acute hepatitis A, PZA was dropped from his regimen to decrease the risk of hepatotoxic reactions.

During his initial visits in the clinic he denied being HIV positive or having risk factors for HIV. His initial CD4 was 200, viral load 10,000. After he tested positive for HIV, he refused to accept his diagnosis. One month into therapy he developed headaches and confusion. He appeared acutely ill with a fever of 104.5 degrees. He was hospitalized and LP demonstrated cryptococcal meningitis. Amphotericin and 5 flucytosine were initiated. Fevers defervesced and his mental status cleared.

Due to the appearance of a second OI it was felt necessary to institute antiretroviral therapy. Efavirenz (Sustiva), stavudine (d4T, Zerit) and lamivudine (3TC, Epivir) were begun. Following last year's CDC TB treatment guidelines Rifampin was changed to Rifabutin to decrease the possibility of drug-drug interactions. Ethambutol was reintroduced to strengthen his anti-TB regimen.

Within a week he again started spiking high fevers. A full evaluation was initiated including CT of the chest and abdomen as well as bone marrow biopsy. No new source of fever was identified. Prednisone therapy was started to treat an immune reconstitution syndrome. DOT of anti-TB medications was continued.

His TB medications were continued for a total of 9 months, during which time he gained 30 pounds. Lymphadenopathy regressed. Chest radiograph cleared. Viral load dropped to a nondetectable level.

*Consultant, RI Dept. of Health

DISCUSSION:

The initial institution of four drug therapy in treating TB is recommended if the local rate of INH resistance is >4%. The four drug regimen prevents the development of further resistance by guaranteeing that the patient is being treated with at least two drugs to which the organism is susceptible.

If, however, there is an epidemiologic risk that the patient may have higher grade primary resistance, more than four drugs should be utilized. INH resistance rates are reported to be at least 25% in Haiti; resistance patterns of other drugs are not available. The IUATLD/WHO resistance study in 1995 did look at the Dominican Republic which shares the same island as

Haiti. In the DR INH resistance is 20%; Rifampin resistance is 16%; Streptomycin resistance is 30%. In addition this patient lived in NYC during the increased incidence of both TB and MDR TB. Thus, a five-drug regimen was initially utilized to ensure adequate coverage pending susceptibility patterns.

When TB and HIV are simultaneously diagnosed, a decision must be made whether to initiate therapy for both diseases simultaneously or in parallel. The decision to treat TB cannot be delayed. Time from infection to death from TB disease in advanced HIV has been demonstrated to be as short as 20 weeks. In addition it has been noted

that treating TB in co-infected individuals can raise CD4 counts and decrease viral load. Institution of concomitant or delayed therapy of HIV must be individualized. In this patient TB treatment was immediately instituted while HIV therapy was delayed. This decision was made for a variety of factors including the fact that the patient would not initially believe he had HIV, making his willingness to comply with HIV therapy unlikely. In addition rifampin, one of most powerful antituberculous drugs, cannot be utilized with NNRTIs or PIs. Whenever possible, rifampin is included in the first two months of TB therapy to improve rapid response.

The development of a second OI (the first OI was TB) changed this situation. Antiretrovirals were instituted, which did necessitate a change in rifamicin use for TB. Reconstitution of the immune system allowed for a dramatic inflammatory response to the patient's TB disease, resulting in a clinical picture of high fevers. Note that immune reconstitution syndrome is a diagnosis of exclusion.

Systemic steroids may be utilized to treat the symptoms of this phenomenon with tapering over 4-6 weeks.

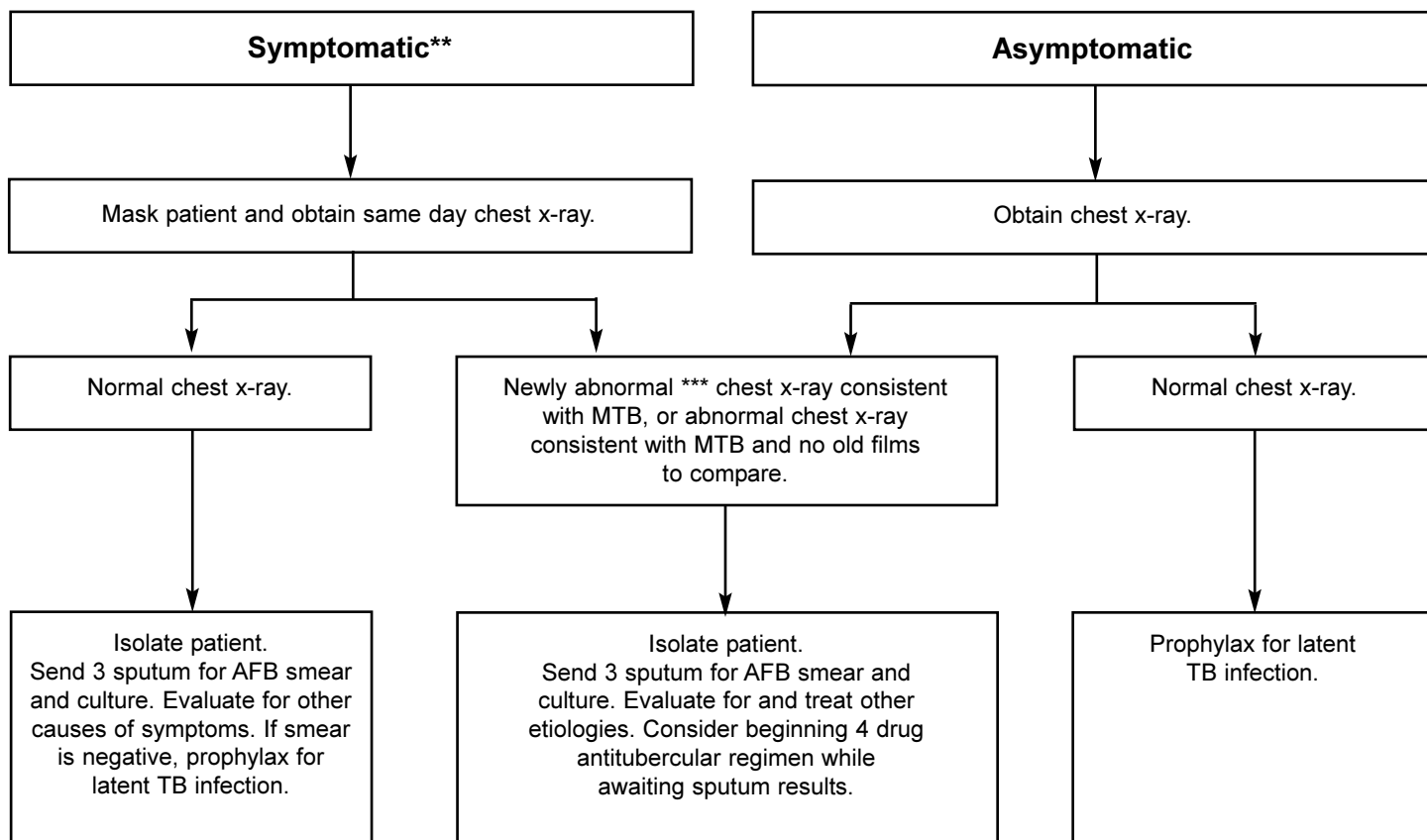
Mistrust, suspicion and fear clearly delayed this patient's diagnosis and affected his early care. Difficulties in his native country led him to pursue a risky escape to the US where he was detained for one year before receiving refugee status. These experiences resulted in mistrust and fear of authority figures. These issues were overcome by a consistent message from his health care providers regarding his care and prognosis. All of these interventions resulted in a good outcome for this gentleman presenting with a constellation of complex, life-threatening conditions.

When TB and HIV are simultaneously diagnosed, a decision must be made whether to initiate therapy for both diseases simultaneously or in parallel.

HEPPIGRAM: Management of a Positive PPD Skin Test

The following is one approach to the incarcerated patient with a newly positive PPD skin test* on routine screening, regardless of HIV status. This algorithm represents an aggressive approach, appropriate to the correctional setting because of:

- 1) congregate living environments, which facilitate the rapid spread of MTB;
- 2) the high prevalence of HIV, much of which is undiagnosed.



*Positive PPD Skin Test is:

- ≥5mm for HIV + patient.
- ≥10mm for HIV- patient.
- an increase of ≥5mm from a prior PPD skin test.
- ≥5mm if patient has a history of TB contact.

**Symptoms include hemoptysis, cough, fever, weight loss, and night sweats.

***Classically, MTB presents with apical infiltrates. In those with HIV infection, the chest x-ray may be normal, or reveal mediastinal adenopathy, or middle/lower lobe infiltrates.

CME IS NOW AVAILABLE ONLINE AT [WWW.HIVCORRECTIONS.ORG](http://www.hivcorrections.org):

HEPP readers are now able to take HEPP News' continuing medical education (CME) tests online at <http://www.HIVcorrections.org>. Any internet browser will enable you to take the HEPP News CME tests every month. Your test results will be registered with the Brown Medical School Office for Continuing Medical Education. When you pass the test, you can either download your CME certificate from the website or request Brown to send the certificate in the mail. Try it out this week!

Interactions between HIV Medications and Rifamycins

Antiretroviral	Rifampin (RIF)	Rifabutin (RFB)
All NRTIs (AZT, 3TC, ddI, ddC, d4T, abacavir)	No significant interaction	No significant interaction
Nevirapine (NVP) <i>Viramune</i>	NVP ↓37% Not recommended	NVP ↓16% No dose change
Delavirdine (DLV) <i>Rescriptor</i>	DLV ↓96% Contraindicated	DLV ↓80%, RFB ↑100% Not recommended
Efavirenz (EFV) <i>Sustiva</i>	EFV ↓25% Possibly ↑EFV dose to 800mg qd	RFB ↓35% Dose change: ↑RFB to 450-600 mg qd or 600 mg 2-3x/week
Ritonavir (RTV) <i>Norvir</i>	RTV ↓35% Dose change: limited data, but probably no change.	RFB ↑400% Dose change: ↓RFB to 150 mg 2-3x week.
Saquinavir (SQV) <i>Invirase/Fortovase</i>	SQV ↓84% Contraindicated for either Invirase or Fortovase, unless using RTV+SQV, then dose RIF 600 mg qd or 2-3x/wk	SQV ↓40% Dose change: contraindicated for Invirase; no adjustment needed for Fortovase, unless using RTV+SQV (with either Invirase or Fortovase), then dose RFB 150 mg 2-3x/week
Nelfinavir (NFV) <i>Viracept</i>	NFV ↓82% Contraindicated	NFV ↓32%, RFB ↑200% Dose change: ↓RFB to 150 mg qd or 300 mg 2-3x/week, ↑NFV dose to 1000 mg tid
Indinavir (IDV) <i>Crixivan</i>	IDV ↓89% Contraindicated	IDV ↓32%, RFB ↑200% Dose change: ↓RFB to 150 mg qd or 300 mg 2-3x/week, ↑IDV to 1000 mg tid
Amprenavir (AMP) <i>Agenerase</i>	APV ↓82% Contraindicated	APV ↓15%, RFB ↑193% Dose change: ↓RFB to 150 mg qd or 300 mg 2-3x/week
Lopinavir/Ritonavir (LPV) <i>Kaletra</i>	LPV ↓75% Contraindicated	RFB ↑300% (25-O-desacetyl metabolite ↑47.5x) Dose change: ↓RFB to 150 mg qd

Sources: Adapted from Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents, Department of Health and Human Services. February 5, 2001: Table 17; and from CDC. Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. MMWR 2000; 49(09):Table 1.

WEBSITES

TB WEBSITES:

National Center for HIV,STD, and TB Prevention
<http://www.cdc.gov/nchstp/tb/>

National Tuberculosis Controllers Association
<http://www.ntca-tb.org/>

Report from the 38th IDSA: Tuberculosis and HIV, by T. R. Sterling, MD
http://www.hopkins-aids.edu/publications/report/nov00_2.html

American Lung Association TB website
<http://www.lungusa.org/diseases/lungtb.html>

American Thoracic Society
<http://www.thoracic.org>

New Jersey Medical School National Tuberculosis Center
<http://www.umdnj.edu/ntbcweb/>

Brown University's TB/HIV Research Laboratory
http://www.brown.edu/Research/TB-HIV_Lab/

World Health Organization Global Tuberculosis Program
<http://www.who.int/gtb/>

HIV TREATMENT WEBSITES:
HIV/AIDS Treatment Information Service
<http://www.hivatis.org>

HIV Insite
<http://hivinsite.ucsf.edu/>

AEGIS: the largest HIV/AIDS resource on the internet
<http://www.aegis.com>

The Body: An AIDS and HIV information Resource
<http://www.thebody.com>

Medscape's Infectious Disease Site
<http://id.medscape.com/>

SAVE THE DATES

TB DATES:

Latent TB Infection: The Hidden Threat in Our Community

San Diego, California

May 5, 2001

Sponsor: American Lung Association of San Diego/Imperial Counties.

Contact: American Lung Association

Call: 619.297.3901

Email: info@lungsandiego.org

CME and CEU credits available

Advisory Council for the Elimination of Tuberculosis

Atlanta, Georgia

July 11-12, 2001

Call: Paulette Ford at 404.639.8008

Email: pbf7@cdc.gov

MORE DATES:

3 Day HIV Minifellowship for Correctional Health Care Providers UTMB at Galveston & Correctional Managed Care

April 23 - 25 and May 21 - 23, 2001

CME credit available

Course fee \$200.00

Call: Penny Welsh at 409.747.8769

Fax: 409.747.8771

Email: pwelsh@utmb.edu

Management of HIV/AIDS in the Correctional Setting: A Live Satellite Videoconference Series

"Management of the HIV/Hepatitis C Co-infected Patient"

June 5, 2001

12:30-3:30 p.m. EST

CME Credits Available through

Albany Medical Center.

Call: 518.262.4674

Email: rosentjh@mail.amc.edu

Visit: www.amc.edu/patient/HIV/hivconf.htm

Infectious Disease Society of America: 39th Annual Meeting

San Francisco, California

October 25-28, 2001

Abstract deadline: May 22, 2001

Late deadline: August 20, 2001

Discounted registration deadline:

July 30, 2001

Fax: 703.299.0204

Visit: www.idsociety.org

The 5th Annual HIV Update: Contemporary Issues in Management

Cambridge, Massachusetts

May 31-June 2, 2001

Call: 617.432.1525

Fax: 617.432.1562

Email: hms-cme@hms.harvard.edu

Visit: <http://134.174.17.108/conted-bin/hmscme>

NEWS FLASHES

Drug Resistant TB on the rise among Foreign-Born persons in the US

A December 2000 JAMA study suggests that TB-infected foreign-born persons are bringing isoniazid-resistant strains of TB into the United States. Researchers from the National Center for HIV, STD, and TB Prevention at the CDC analyzed data from case reports submitted to the CDC's national TB surveillance system from 1993 to 1998. Dr. Elizabeth Talbot and colleagues predict that more than half of TB cases in the US may occur among foreign-born people by the year 2002. (Talbot E, Moore M, McCray E, Binkin N. JAMA, 2000; 284: 2894-2900.)

Serostatus Approach to Fighting the Epidemic (SAFE)

At the recent 8th Conference on Retroviruses and Opportunistic Infections, the Centers for Disease Control and Prevention (CDC) announced a new national approach to providing HIV prevention services, the Serostatus Approach to Fighting the Epidemic (SAFE). The goal of SAFE is to raise the importance of focused prevention efforts to ensure early knowledge of HIV infection, and expand prevention support and treatment for persons living with HIV. By increasing the number of people getting tested, enrolled in primary care programs, and committed to state of the art HIV treatment, SAFE hopes to reduce HIV transmission rates by 50% by the year 2004 (from 40,000 new infections per year to 20,000). Robert Janssen, MD, Division Director of the National Center for HIV/AIDS, STDs and TB Prevention's (NCHSTP) Division of HIV/AIDS Prevention, has stated that correctional populations would be important intervention sites for SAFE's programs. (For more information on SAFE, contact Karina Krane, 404-639-8862).

HIVMA's New Requirements for HIV Specialists

The HIV Medicine Association (HIVMA), a division of The Infectious Diseases Society of America, has developed requirements for

physicians seeking to become qualified in the treatment of patients with HIV. HIVMA hopes that their regulations will ensure that patients with HIV disease receive the highest quality of care, reflecting current medical research, at the hands of those who have demonstrated experience and commitment to treating this disease. While HIVMA does not require HIV-qualified physicians to be of a specific medical discipline, the group does stipulate that a physician must have managed at least 25 patients with HIV infection in the last year and have spent at least 15 hours on HIV-related continuing medical education. Recently trained, certified, or recertified infectious disease specialists are also considered qualified providers. (For more information, visit the HIVMA site at: <http://www.hivma.org>)

Prison Health Services to take over Health Care in New York City Corrections

On January 1 of this year, Prison Health Services (PHS), one of the nation's largest profit-making providers of inmate medical care, replaced St. Barnabas Medical Center of the Bronx as care provider for the 13,500 inmates in New York City correctional facilities. St. Barnabas has been the subject of frequent criticism, and a criminal investigation by the Manhattan district attorney's office following several inmate deaths. New York City has created a strict contract with PHS, demanding that they agree to stringent staffing requirements, heightened standards of care, and steep financial penalties for any failures. Under the deal, prenatal exams, dental work and AIDS care must be provided faster; medications must be provided within 24 hours of when they are first prescribed. PHS will provide basic care to inmates at the Rikers Island jails, the Manhattan Detention Complex and the Vernon C. Bain floating jail. PHS will deliver care by mental health professionals, dentists, and other specialties, but treatment for serious injuries and emergencies will be provided at city-owned hospitals. (Lipton E. New York Times, 12/1/2000.)

RESOURCES

Safety First: HIV Prevention for Correctional Professionals

A video and brochure entitled "Safety First: Steps You Can Take to Protect Yourself Against On-the-job Exposure to HIV and Hepatitis" is now available in Spanish and English to help correctional employees protect themselves from the threat of infection on the job. To order, fax a request to Agouron at 562.658.2192, or call 800.311.3435.

If you know of other such educational resources, please send information to the attention of Betsy Stubblefield at HEPP News.

SELF-ASSESSMENT TEST FOR CONTINUING MEDICAL EDUCATION CREDIT

Brown Medical School designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through July 31, 2001. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Which of the following is not considered a positive skin test for TB infection?
 - a) ≥5mm for HIV+ patient.
 - b) ≥5mm for a patient with a history of TB contact.
 - c) ≥10mm for HIV- patient
 - d) increase less than 5mm from previous PPD.
 - e) all of the above are positive skin tests for infection.

2. Indicate which of the following sentences are true?
 - a) All inmates should be screened for TB signs or symptoms at intake.
 - b) Inmates known to have HIV infection should have a chest radiograph as part of the initial screening, regardless of their TST status
 - c) Tuberculin skin tests (TST) should be administered to all prisoners who have not had a previous documented positive skin test result.
 - d) a and b.
 - e) All of the above
 - f) None of the above

3. Which of the following antiretrovirals may be acceptable for co-administration with rifampin?
 - a) Nelfinavir (NFV, Viracept)
 - b) Delavirdine (DLV, Rescriptor)
 - c) Efavirenz (EFV, Sustiva)
 - d) Indinavir (IDV, Crixivan)
 - e) a and b
 - f) All of the above.

4. Which of the following antiretrovirals is not recommended for co-administration with rifabutin?
 - a) Saquinavir (SQV, Fortovase, Invirase)
 - b) Nelfinavir (NFV, Viracept)
 - c) Amprenavir (AMP, Agenerase)
 - d) Nevirapine (NVP, Viramune)
 - e) Delavirdine (DLV, Rescriptor)
 - f) All of the above.

5. In which of the following situations is hepatotoxicity considered a threat?
 - a) patients taking isoniazid or pyrazinamide
 - b) patients on fluconazole
 - c) patients with a history of injection drug use
 - d) a and b
 - e) a and c
 - f) All of the above

6. Which of the following statements are true about TB treatment?
 - a) The initial use of four drug therapy in treating TB is recommended if the local rate of INH resistance is >4%.
 - b) Treating TB in co-infected individuals improves can raise CD4 counts and decrease viral load.
 - c) Malabsorption of antituberculous medications has been demonstrated to occur in HIV disease and in diabetes.
 - d) a and b
 - e) All of the above

HEPP NEWS EVALUATION

5 *Excellent* 4 *Very Good* 3 *Fair* 2 *Poor* 1 *Very Poor*

1. Please evaluate the following sections with respect to:

	educational value	clarity
Main Article	5 4 3 2 1	5 4 3 2 1
HEPPigram	5 4 3 2 1	5 4 3 2 1
HIV 101	5 4 3 2 1	5 4 3 2 1
Save the Dates	5 4 3 2 1	5 4 3 2 1

2. Do you feel that HEPP News helps you in your work? Why or why not?

3. What future topics should HEPP News address?

4. How can HEPP News be made more useful to you?

5. Do you have specific comments on this issue?

BROWN MEDICAL SCHOOL • OFFICE OF CONTINUING MEDICAL EDUCATION • BOX G-A2 • PROVIDENCE, RI 02912

The Brown Medical School is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education activities for physicians.

The use of the Brown Medical School name implies review of the educational format and material only. The opinions, recommendations and editorial positions expressed by those whose input is included in this bulletin are their own. They do not represent or speak for the Brown Medical School.

For Continuing Medical Education credit please complete the following and mail or fax to 401.863.2660 or register online at www.hivcorrections.org. Be sure to print clearly so that we have the correct information for you.

Name _____ Degree _____

Address _____

City _____ State _____ Zip _____

Telephone _____ Fax _____