2-2005

IDCR: Infectious Diseases in Corrections Report, Vol. 8 No. 2

Infectious Diseases in Corrections

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INFECTIOUS DISEASES IN CORRECTIONS REPORT

FORMERLY HEPP Report

Feb. 2005 Vol. 8, Issue2

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ABOUT IDCR

IDCR, a forum for correctional problem solving, targets correctional physicians, nurses, administrators, outreach workers, and case managers. Published monthly and distributed by email and fax, IDCR provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, as well as efficient ways to administer treatment in the correctional environment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education. IDCR is distributed to all members of the Society of Correctional Physicians (SCP) within the SCP publication, CorrDocs (www.corrdocs.org).

SUPPORTERS

IDCR is grateful for the support of the following companies through unrestricted educational grants:
Major Support: Abbott Laboratories, Boehringer Ingelheim and Roche Pharmaceuticals.
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IDCR MISSION STATEMENT

We changed our name from HEPP Report to IDCR (Infectious Diseases in Corrections Report) to encompass all infectious diseases that impact the correctional setting. IDCR's goal is to educate correctional health care providers about the appropriate medical management of prisoners infected with HIV, hepatitis, TB, and other infectious diseases; to encourage these providers to improve their networks with correctional, academic or community-based infectious disease experts; and to promote a level of infectious disease care in correctional facilities that is equivalent to the "community standard."

TUBERCULOSIS OUTBREAK AMONG STAFF IN CORRECTIONAL FACILITIES, FLORIDA, 2001-2004: LESSONS RE-LEARNED

David Ashkin, MD, Florida Department of Health*
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- The prevalence of latent tuberculosis infection (LTBI) among prison inmates is four times higher than the prevalence in the general population.
- The prevalence of LTBI among jail inmates is 17 times higher than the prevalence in the general population.
- More than 500,000 inmates with LTBI are released nationwide every year.
- The rate of tuberculosis (TB) infection in jails is 15 times that seen in the general population.
- One-third of those with active TB in this country have been recently incarcerated[1,2].

While most prisons and jails are vigilant when it comes to screening for TB infection, some correctional facilities are not attentive to LTBI treatment completion, thereby providing an ideal condition in which TB outbreaks may occur. When a TB outbreak occurs, public health officials should initiate an investigation of the circumstances related to the outbreak and try to interrupt further transmission of *Mycobacterium tuberculosis* (*M. tuberculosis*). This report of a recent TB outbreak in two Florida correctional facilities illustrates the complexities of TB control in congregate settings and highlights the need for further improvements in TB control measures in prisons and jails.

The TB Outbreak Setting

The local Health Department, in consultation with the Florida Bureau of TB and Refugee Health (FBTBRH), and the Florida Department of Corrections, investigated an outbreak of drug-susceptible TB that occurred among staff at two closely situated correctional facilities (facilities A and B) during the period April - September 2004.

Facility A has an inmate population of 875 and 343 work camp inmates. Correctional personnel working at the facility include 363 correctional staff, 26 medical personnel, and 13 contracted food workers. Facility B is located ten miles south of facility A. This facility incarcerates 1,361 inmates, and 216 correctional staff and 38 medical personnel work at the facility. Some of the correctional facility employees periodically rotate between the two facilities.

Approach to the Outbreak Investigation

The investigation of the outbreak was conducted in 2004 and standard TB case-based follow-up methods were used. The index patient was defined as the first patient to receive a

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WHAT'S INSIDE

TB OUTBREAK… ***(cont. from page 1)***

diagnosis of TB, regardless of location of that case. The outbreak period was defined as the time period commencing when the index case reported TB-associated symptoms, and concluding one week after the last infectious patient was placed in respiratory isolation. The potentially infectious period for each patient was defined as commencing on the date of onset of symptoms consistent with TB or if no symptoms, 12 weeks from the date of diagnosis, and concluding when the patient was isolated from further contact with others. *M. tuberculosis* isolates from case patients were fingerprinted by IS-6110 restriction fragment length polymorphism (RFLP) to determine if cases were caused by the same strain. A case was included in the outbreak if there was a history of close contact, defined as shared cells or work area with another case linked to the outbreak, and/or if the subject's *M. tuberculosis* isolate had a matching RFLP fingerprint.[i]

All inmates and staff were questioned regarding TB risk factors and tuberculin skin tests (TSTs) were administered to all inmates and staff, excluding members of the staff who had a previously documented positive test or those who had a negative test within the past three months.[ii] (see TB 101, page 7.)

A positive TST was defined as induration greater or equal to 5 mm. Inmates who had positive TST results or symptoms suggestive of TB, regardless of TST results, were evaluated with a chest radiograph. (see IDCR-o-gram, page 6) The chest radiographs were conducted at the on-site medical units. Correctional staff members who had a positive TST or symptoms suggestive of TB were referred to the local DOH TB clinic for chest radiograph, medical evaluation, and treatment.

Three sputum samples were obtained from every inmate or staff member who demonstrated signs and symptoms suggestive of TB. Sputum smears were examined for acid-fast bacilli (AFB), were cultured for mycobacteria, and the *Mycobacterium tuberculosis* direct (MTD) test was performed.[iii] Correctional staff members who had a positive TST ≥5MM or symptoms suggestive of TB were sent to the local health department for evaluation. Inmates who were suspected of having TB were placed in negative airborne infection isolation rooms at the facility.

Results of the 2004 Outbreak Investigation

The 2004 outbreak investigators discovered that over a period of two and a half years (May 2001-September 2004), five cases of TB were reported among correctional staff members working at facilities A or B. Of these five cases, four cases of TB were identified among the correctional staff members at facility A and one case of TB was identified in a correctional staff member who worked at facility B. Cases 2 and 4 from facility A, and Case 3 from facility B were linked to the index case by RFLP fingerprinting of isolates and contact exposure history. Case 5 from facility A was epidemiologically linked to the other four cases, however the RFLD fingerprint did not match with the other cases.

> The single most potent factor affecting the risk of progression from LTBI to TB disease is HIV coinfection.

The index case, identified as the source case, was an HIV-infected staff member initially diagnosed with extrapulmonary TB in May 2001. This patient was employed as a secretary in the medical unit in facility A and had frequent contact with coworkers and correctional officers who were involved in the transportation of inmates. A private physician managed TB treatment, TB medications were self-administered,[iv] and the patient was found to be non-adherent with the medications. No contact investigation was performed when the patient was first diagnosed in 2001 since the patient was felt to have only extrpulmonary TB and therefore, was considered to be "non-infectious".[v] However, in September 2002, despite the fact that the patient originally was noted to have had a cough. At this time, pulmonary TB was diagnosed (see Table 1, page 3.) and a contact investigation in facility A was conducted. A review of the patient's medical records revealed that sputum specimens were not obtained prior to September 2002.

Case 2, an HIV-uninfected correctional transportation officer employed at facility A, was identified during the September 2002 contact investigation. This individual had a previously documented positive TST and a previous history of TB that could not be varified. Symptoms suggestive of TB were not recorded in 2002, but a private physician who was providing treatment ordered a chest radiograph.[vi] The chest radiograph demonstrated an infiltrate and sputum specimens were positive for AFB on smear and *M. tuberculosis* in culture. Additional investigations were not conducted, as the contact investigation around the index case was deemed sufficient to capture this case's workplace contacts.

Case 3, an HIV-uninfected correctional transportation officer employed at facility B, was diagnosed with pulmonary TB in October 2002. This individual was responsible for transporting inmates to and from the medical units of facilities A and B. Case 3's sputum specimen was positive for both AFB on smear and *M. tuberculosis* in culture.

Case 4, an HIV-uninfected correctional transportation officer employed at facility A, was diagnosed with TB in March 2004. A private physician monitoring this subject for a history of asthma ordered a chest radiograph in 2004 for reasons unrelated to the TB outbreak. The chest radiograph revealed a 1 cm nodule in the right upper lobe. Tissue culture obtained following excision of the upper lobe nodule was positive for *M. tuberculosis*. Case 4 was initially identified as a contact to the index case but did not follow through with medical evaluation and treatment. Additionally, this subject was a TST converter; his baseline TST measured 0 mm in 2002 and 10 mm in August 2003.[vii] The RFLP pattern confirmed the link between this case, the index case, and cases 2 and 3.[viii]

Case 5, an HIV-uninfected correctional officer employed at facility A was diagnosed with pulmonary TB in April 2004. This case's RFLP fingerprint did not match the RFLP fingerprint obtained for the index case or cases 2, 3, or 4, but an epidemiological link was identified as this case had close social contact with Case 4.[ix]

Records on skin tests and/or TST records, results, and chest radiographs were not available for the majority of correctional staff at both facilities.

The clinical characteristics of the index patient and the secondary cases (Cases

Continued on page 3

Table 1. Clinical characteristics of the index patient and the secondary cases (Cases 2, 3, 4 and 5)

Case	Date Reported	Sputum AFB Smear Results	Culture Results	Chest Radiograph	Signs/ Symptoms	DNA Match	Comments
Index Case	History of treatment for extra-pulmonary TB in 5/00; culture positive pulmonary TB in 9/02	Smears not done 2000 Positive 2002	MTB+*	Abnormal	Cough	Yes	Health care secretary at facility A; HIV infected; frequently received visits from transportation officers
2	10/02	Positive	MTB+	Infiltrates in Right Upper Lobe	Night sweats	Yes	Transportation officer at facility A; HIV uninfected
3	10/02	Negative	MTB+	Abnormal	Intermittent Cough	Yes	Transportation officer at facility B; HIV uninfected
4	3/04	Negative	No culture performed	Non-cavitary but consistent with TB	Cough	Yes	Transportation officer at facility A; HIV uninfected
5	4/04	Positive	MTB+	Non- cavitary but consistent with TB	Cough	No	Correctional officer at facility A; HIV uninfected

**MTB+ - Culture was positive for M. tuberculosis*

TB OUTBREAK... *(cont. from page 2)*

2, 3, 4 and 5) are listed in Table 1, page 3.

Outbreak Investigation

During the 2004 outbreak investigation, all movement in and out of both facilities, including visitation, was halted for one week, to allow initial screening of all inmates and correctional officers. During that one week 78 staff received TSTs and all staff and inmates were screened using a symptom screen and risk assessment.[x] Of the staff screened/tested, 54 of these individuals were referred to the local health department TB clinic for evaluation of symptoms suggestive of TB or for follow-up evaluation of a positive TST. TSTs were performed on all inmates with a history of a negative TST and chest radiographs were obtained for 30 inmates to further evaluate symptoms suggestive of TB or because they had a positive TST. Sputum specimens were obtained from 18 inmates who had abnormal chest radiographs and/or symptoms suggestive of TB.

Follow up

As a result of this outbreak, the state and local health departments recommended implementation of an electronic database for tracking serial TB screenings so that TST conversions and appropriate recommendation of follow-up medical care will be documented. This is the recommended practice in all high risk settings, such as medical and correctional facilities[3]. Quarterly skin testing of inmates and correctional staff at these facilities will continue until no further conversions are identified. At the time of this publication, no further active cases of TB disease have been identified.

Discussion and Recommendations for Florida Outbreak

Several lines of evidence suggest that *M. tuberculosis* was transmitted from the index patient to correctional staff at facilities A and B. The index case was a medical staff member employed in the health care unit at facility A, who had been diagnosed with extrapulmonary TB in 2001. This patient was not adherent with self-administered treatment and worked with several correctional transportation officers. Since an evaluation for pulmonary TB was not performed in May 2001 (the time of initial diagnosis), it is not clear if this individual was infectious at this time. This individual developed symptoms of pulmonary TB in 2002, and may have infected other correctional staff from January 2001 to June 2002.

The long duration of exposure to the source (index) case is also attributable to a failure to monitor the patient's adherence with anti-TB treatment. Noncompliance with TB treatment is a well-known problem[4]. All TB medications should be administered by directly observed therapy and adherence documented, as this is the current standard of care[3]. Public health consultants and staff are available to assist with TB case evaluation and adherence with anti-TB medication.

Furthermore, since records on TSTs and/or chest radiographs were not available for the majority of the correctional staff, it was difficult to ascertain correctional staff compliance with annual TSTs. TST conversions could not clearly be related to the period of exposure. Obtaining baseline TSTs in higher risk settings, such as medical and correctional facilities, is generally recommended,[iii] as it provides a point of reference for measurement of TST conversion rates.

Although mandatory screening and testing of all employees had been implemented three years prior to this outbreak, several correctional staff members did not comply. Correctional supervisors must be able to identify employees who are not compliant to such policies and implement appropriate education and corrective actions if these policies are not adhered to. Measures need to be supported (with collaboration to help design, implement, and monitor) by public health programs to address conditions, which foster the transmission of *M. tuberculosis*, identify corrective measures, and implement and monitor all follow-up.

Continued on page 4

TB OUTBREAK... *(cont. from page 3)*

Employers are unlikely to be aware of the HIV status of their employees. Educational programs for both inmates and staff are essential for the protection of all persons at the facility. All staff (and therefore the potentially unknown HIV-infected or immunosuppressed staff) should be repeatedly advised of the increased risk with regard to TB in those with HIV infection, the importance of TB skin testing and completion of LTBI treatment, and should be taught to recognize symptoms of TB. Practitioners treating correctional personnel and inmates should have a high index of suspicion for TB and obtain appropriate smears and cultures whenever possible.

General Discussion and Recommendations

There is a dangerous synergy between HIV and TB. Prisoners, who have long been known to have disproportionately high rates of TB disease and TB infection,[v] also have more than five times the general population's rate of AIDS, and between four and 10 times the general population's rate of HIV infection[6]. The single most potent factor affecting the risk of progression from LTBI to TB disease is HIV coinfection[7]. It is often more difficult to detect TB in persons with HIV/AIDS because they may not respond to the TST, and may present with atypical or negative findings on chest radiographs[8]. It is therefore recommended that HIV-infected patients with respiratory symptoms undergo a sputum analysis in addition to a chest radiograph. Furthermore, significant drug interactions may complicate the concurrent treatment of HIV and TB[9]. 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.

As recommended by the National Commission on Correctional Health Care (NCCHC), all inmates should receive TB 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. TSTs should be administered to all inmates and correctional staff members who have not had a previous documented positive TST result. (see IDCR-o-gram, page 6.) Any patient whose TST indicates TB infection should receive a chest radiograph. TST may fail to identify TB infection in high-risk patients including inmates[10] - TB control officers may consider using on-site chest radiography to screen all inmates at entry.

Inmates and correctional staff who have documented LTBI should complete a course of treatment and adherence should be monitored[3]. Those with a positive TST who cannot complete treatment for LTBI should receive regular screening for TB symptoms; any such patient with significant immune compromising factors should be scrutinized for TB symptoms even more frequently. Inmates who do not present with TB upon initial intake screening should be evaluated annually for TST conversion, and more frequently if there is evidence of recent transmission of *M. tuberculosis* in the facility, or if inmates with HIV are housed together[11].

As an airborne infection, TB presents one of the most prescient threats not only to inmates, but also to correctional staff, health care providers, visitors, and others who come in close contact with TB patients. This case illustrates that point - one more time.

DISCLOSURES: **Nothing to disclose*

NOTES:

i. RFLP analysis is a DNA fingerprinting method that allows public health officials to distinguish the transmission of specific strains of tuberculosis during an outbreak. This method is based on the detection of the copy number and location of the mobile genetic element IS6110 in the M. tuberculosis genome. Enzymatic digestion of the DNA produces fragments, which can be separated by electrophoresis. The fragments are immobilized on a nylon membrane, and a specific chemoluminescence-labeled DNA probe is used to reveal the pattern bands on x-ray film.

ii. Best practice would be to test every individual who had a negative PPD test at the time of the outbreak investigation. However, this practice can be difficult to enforce with correctional staff. Additional education regarding TB exposure, testing and management could improve TST uptake among correctional personnel.

iii. MTD tests are isothermal transcription-mediated amplification assays used in the rapid identification of M. tuberculosis in respiratory samples. These tests produce results within two to seven hours after sputum processing.

iv. Best practice would be to have this patient take TB medications under directly observed therapy, especially given the patient's history of immunosuppression.

v. HIV-infected subjects who have extrapulmonary tuberculosis can have undetected pulmonary infection. In general, no patient with suspected tuberculosis can be considered non-infectious until sputum smears are also found to be negative; in the case of HIV-infected patients, culture for TB should also be performed, as sputum smears may be negative, despite the presence of active pulmonary tuberculosis.

vi. Any individual who has a positive TST, with or without the presence of symptoms suggestive of TB, should have a baseline chest radiograph.

vii. Best practice would have been to perform a chest radiograph at the time of TST conversion.

viii. Active tuberculosis should be considered whenever any individual who works in a higher risk setting, such as a medical facility or correctional facility, presents with a pulmonary infiltrate. TST should be performed and sputum specimens should be obtained for AFB smear and culture.

ix. There can be "background" cases even in the face of an outbreak. These types of cases could possibly be the next source case of a future outbreak. Vigilance for anyone with symptoms suggestive of TB need to be identified and evaluated early.

x. Best practice is to perform risk assesment, symptom screening and TSTs on all staff. However, staff have the right to refuse testing on-site and may receive TSTs from private physicians.

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Letter from the Editor

This month we bring you an exciting tale of a TB outbreak in a correctional setting; Drs. David Ashkin, Jean Malecki, and David Thomas report on a tuberculosis outbreak among staff in two Florida correctional facilities. Outbreaks are invariably caused by lapses in tuberculosis control, where a case of infectious pulmonary tuberculosis has been unrecognized or inappropriately managed. Recognition or suspicion of an outbreak may be through diagnosis of the index case, evidence of clustering of cases or positive tuberculin skin tests, or unusual trends in epidemiologic data, as shown in this example.

Outbreak investigations should include case finding and identification of exposed contacts so that tuberculin skin testing and screening for tuberculosis disease can be performed. Contact investigations are usually performed using a concentric circle approach, where contacts with the greatest exposure, such as household members, are identified and tested. If the rate of *Mycobacterium tuberculosis* infection is greater than expected, the investigation should move to the next highly exposed circle of contacts, such as work or school contacts. Subsequent concentric circles of contacts should be tested until the rate of infection is thought to be equal to that of the surrounding community.

Outbreaks represent experiments of nature, and while the first duty is interruption of transmission and identification and testing of exposed contacts, outbreaks also are an opportunity to learn valuable lessons. Examining missed opportunities that may have lead to the outbreak can point out areas within a tuberculosis control program in need of improvement or strengthening. This is clearly the case for the Florida Department of Corrections, and important steps have been taken to improve TB control.

In addition, new information about the pathogenesis and transmission of *M. tuberculosis* can be learned from outbreak investigations. Examples of lessons learned from outbreak investigations include that children, who were thought not to transmit infection, can be highly infectious; that *M. tuberculosis* can be transmitted through improperly disinfected bronchoscopes; and that in those with HIV infection, the time to development of tuberculosis disease after infection is accelerated when compared to those without HIV infection. In all cases, suspected outbreaks of tuberculosis should be reported promptly to public health authorities and investigations should be performed in conjunction with state and local tuberculosis control programs.

The algorithms included in this issue depict how to proceed when someone presents with suspected TB in the correctional setting, and the TB 101 details how to classify the tuberculin skin test reaction. At the conclusion of this issue, readers will be more familiar with TB treatment guidelines and how to prevent TB outbreaks in the correctional setting, know more about who should be tested for tuberculosis, and be aware of different tuberculin skin test reactions, and their implications. Let's all hope that this TB update prevents a few outbreaks of TB in the future.

Sincerely,
Renee Ridzon, MD

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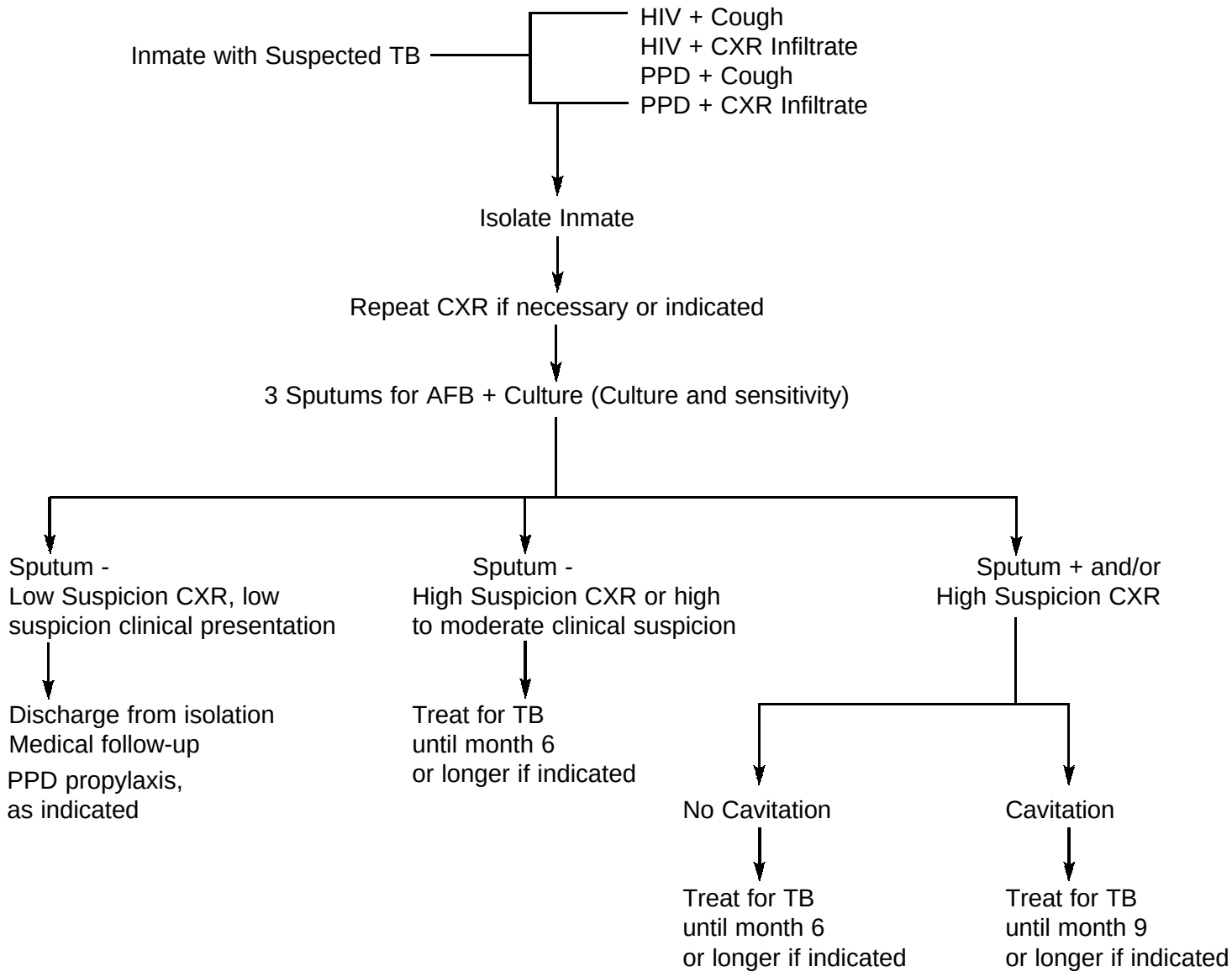
Faculty Disclosure

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 and hepatitis unless otherwise indicated. For the treatment of HIV and hepatitis infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

IDCR-O-GRAM: Suspected TB in the Correctional Setting



All TB treatment begins with isoniazid, rifampin, pyrazinamide, and ethambutol for the initial 2 months. A repeat smear and culture should be performed after 2 months of treatment. Normally, the continuation phase of treatment should consist of isoniazid and rifampin daily or twice weekly for 4 months to complete a total of 6 months of treatment. If cavitation was present on the initial chest radiograph and the culture at the time of completion of 2 months of therapy is positive, the continuation phase should be lengthened to 7 months (total of 9 months of treatment).

If the patient has HIV infection and CD4 <100/ul, the continuation phase should consist of daily or three times weekly isoniazid and rifampin. In HIV-uninfected patients having no cavitation on chest radiograph and negative AFB smears at completion of 2 months of treatment, the continuation phase may consist of either once weekly isoniazid and rifapentine, or daily or twice weekly isoniazid and rifampin, to complete a total of 6 months. Patients receiving isoniazid and rifapentine, and whose 2 months cultures are positive, should have treatment extended by an additional 3 months (total of 9 months).

TB 101

Who Should Be Tested for TB

- People with HIV infection (the AIDS virus)
- People in close contact with those known to be infectious with TB
- People with medical conditions that make the body less able to protect itself from disease (for example: diabetes, the dust disease silicosis, or people undergoing treatment with drugs that can suppress the immune system, such as long-term use of corticosteroids)
- Foreign-born people from countries with high TB rates
- Some racial or ethnic minorities
- People who work in or are residents of long-term care facilities (nursing homes, prisons/jails, some hospitals)
- Health care workers and others such as prison guards
- People who are mal-nourished
- Alcoholics and IV drug users

CDC. Division of Tuberculosis Elimination. Available at: http://www.cdc.gov/nchstp/tb/faqs/qa_latenttbinf.htm#Infection1

When is a Tuberculin Skin Test (TST) Reaction Positive?

5 or more millimeters	**10 or more millimeters**	**15 or more millimeters**
An induration of 5 or more millimeters is considered positive for: ◆ People with HIV infection ◆ Close contacts ◆ People who have had TB disease before ◆ People who inject illicit drugs and whose HIV status is unknown	An induration of 10 or more millimeters is considered positive for: ◆ Foreign-born persons ◆ HIV-negative persons who inject illicit drugs ◆ Low-income groups ◆ People who live in residential facilities (nursing homes, prisons/jails) ◆ People with certain medical conditions ◆ Children younger than 4 years old ◆ People in other groups as identified by local public health officials	An induration of 15 or more millimeters is considered positive for: ◆ People with no risk factors

Adapted by IDCR from CDC. Division of Tuberculosis Elimination.

RESOURCES

NEW! Treating the HIV and TB Co-infected Patient in the Correctional Setting course
Available at: www.umdnj.edu/ntbcweb/hivtbcd.htm

CDC Division of Tuberculosis Elimination Fact Sheets
Available at: www.cdc.gov/nchstp/tb/pubs/dtbefax.htm

Charles P. Felton National TB Center at Harlem Hospital.
Addressing HIV/AIDS Issues in TB Contact Investigation: A Guide for Contact Investigators, Managers, and Trainers. 2004.

Charles P. Felton National Tuberculosis Center at Harlem Hospital
Improving Treatment Completion for Latent Tuberculosis Infection Among Health Care Workers. 1999.

Save the Dates

Conference on Retroviruses and Opportunistic Infections
February 22-25, 2005
Boston, MA
Visit: www.retroconference.org/2005

IUALTB Challenges to TB Control
February 23-26, 2005
Vancouver, British Columbia, Canada
Call: 604.732.5864
Email: biagtan@bc.lung.ca

Improving the Management of HIV Disease Regional CME Courses
Atlanta, GA: March 11, 2005;
New York, NY: March 17, 2005;
Los Angeles, CA: April 16, 2005;
Chicago, IL: May 2, 2005;
Washington, DC: May 2005;
San Francisco: May or June 2005:
Registration for this course will open soon.
Visit: www.iasusa.org/registration/index.html

Management of HIV/AIDS in the Correctional Setting: A Live Satellite Videoconference Series "The Triply Diagnosed Patient: HIV, Mental Health & Substance Use"
March 9, 2005
12:30-2:30 p.m. EST
Call: 518.262.4674
Email: ybarraj@mail.amc.edu
Visit: www.amc.edu/patient/hiv/hivconf/index.htm

World TB Day
March 24, 2005
Visit: www.cdcnpin.org/scripts/spotlight/spot_wtd05.asp for World TB Day activities

ACHSA Diminishing Resources: The New Reality
March 31-April 3, 2005
Oakland, CA
Visit: www.achsa.org

NCCHC Updates in Correctional Health Care
April 9-12, 2005
Las Vegas, Nevada
Visit: www.ncchc.org

AMFAR National HIV/AIDS Update Conference
April 10-13, 2005
Oakland, CA
Visit: www.amfar.org

In The News

Study Details Effects of ART on Liver Disease
Liver disease has emerged as a leading cause of death among persons co-infected with HIV and HCV. A recent study estimated the burden of liver disease and evaluated determinants of liver fibrosis and necroinflammatory activity among HIV/HCV co-infected patients receiving antiretroviral therapy (ART). One-hundred twelve randomly selected and 98 referred HCV-infected patients undergoing care in an HIV clinic were studied. All patients had liver biopsies performed between April 2001 and July 2002, and had not received treatment for HCV infection prior to biopsy. Sixty-four percent of patients were receiving ART at the time of liver biopsy and 12% of patients had a previous episode of grade 3 or 4 ART-associated liver enzyme elevation. No hepatic fibrosis was detected in 33% of individuals, 41% had fibrosis restricted to the portal tracts, and bridging fibrosis and cirrhosis were noted in 9% and 17% of individuals, respectively. The median necroinflammatory activity score was 3, and 58 individuals had activity scores of 5 or higher. Individuals with persistently elevated ALT and/or AST levels, defined as having more than 1 in every 3 ALT or AST measurements >100ul, had a five-fold greater risk of bridging fibrosis or cirrhosis, compared with persons with lower liver enzyme levels. While this study found no evidence that ART caused serious histological liver disease, it was found that individuals with longer cumulative exposure to ART had significantly less necroinflammatory activity.
Hepatology. 41(1); January 2005.

FDA Approves New 500mg Invirase
The FDA recently approved a new 500mg, film-coated tablet formulation of the HIV protease inhibitor Invirase (generic name, saquinavir), designed for use in combination with ritonavir and other anti-HIV drugs for the treatment of HIV infection. The approval was based on data that show that similar drug levels are achieved with Invirase 500mg tablets and Invirase 200mg tablets, when each is administered with ritonavir 100mg and taken with food. The new formulation of Invirase will reduce pill count from five pills to two, twice daily, in hopes of improving patient adherence.
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Research: Low Rate of Treatment Failure with Tenofovir, Lamivudine, Zidovudine
Triple NRTI regimens combining tenofovir, lamivudine (3TC), and abacavir or didanosine have recently shown high rates of virologic failure, most often associated with the K65R resistance mutation. However, the inclusion of zidovudine may be protective against virologic failure and selection of the K65R mutation. Data was collected retrospectively from 40 patients who had previously been prescribed ART consisting of tenofovir, 3TC, and zidovudine. Baseline was considered the time immediately before each patient switched to the ART regimen consisting of tenofovir, 3TC, and lamivudine. At baseline, 27 patients' (group 1) HIV RNA levels were undetectable (<50 copies/ml) and 13 patients (group 2) had detectable HIV RNA levels ranging from 200-398,000 copies/ml. At the time of analysis, all patients had completed at least 24 weeks after initiation of treatment. Upon analysis, HIV RNA level was less than 50 copies/ml in 23 of 27 patients who had undetectable HIV RNA at baseline, and in 8 of 13 patients with detectable HIV RNA levels at baseline. The median CD4 cell counts in group 1 and 2 increased from 415 cells/ul to 595 cells/ul and from 354 cells/ul to 407 cells/ul, respectively. All nine patients who showed a virologic failure on tenofovir, 3TC, and lamivudine were genotyped for resistance. Two patients admitted to not having taken medication regularly. Of the seven remaining patients, the K65R mutation was detected in only one patient.
AIDS. 19(1); January 2005.

FDA Recommends Not Using Indinavir in Pregnant Women
The clinical pharmacology section of the Crixivan (Indinavir, IDV) label has been revised to include pharmokinetic data from a study in HIV-infected pregnant women, that showed results of significantly reduced IDV concentrations in women at 30-32 weeks gestation compared to levels post-partum. Based on these data, IDV is not recommended in HIV-infected pregnant patients.
FDA issued report; Dec 27, 2004.

CDC Recommends HIV Drugs for All Those Exposed
The CDC recently issued new recommendations that people exposed to HIV from non-occupational exposure, such as sexual assault, accidents, occasional drug use, or unsafe sex, receive antiretroviral medications to stave off HIV infection. Previously, the recommendations for emergency drug treatment were only for healthcare workers who with parenteral exposure through needlestick injuries, splashed to mucous membrane, or other occupational exposure. This recommendation was first made in 1996. However, the CDC has stated that "the severity of the HIV epidemic dictates we use all available tools to reduce infection." The new approach, called non-occupational post-exposure prophylaxis (NPEP) involves taking a daily antiretroviral regimen, which must begin within 72 hours after exposure and continue for 28 days. While NPEP is an important expansion of current HIV prevention strategies, it should not be viewed as the first line defense against HIV.
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Self-Assessment Test for Continuing Medical Education Credit

Brown Medical School designates this educational activity for one hour in category one 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, 2005. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. A TST is considered positive at 10 mm or more for the following persons:
   A. Children younger than 5 years old
   B. Inmates
   C. People with HIV infection
   D. A and B
   E. All of the above

2. The following statements about RFLP are all true, except:
   A. RFLP stands for restriction fragment life polymorphism
   B. RFLP detects the copy number and location of the IS6110 element in the M. tuberculosis genome.
   C. RFLP was used in the Florida TB outbreak investigation to link cases.
   D. During RFLP analysis, DNA is enzymatically digested to produce DNA fragments, which can then be separated by electrophoresis.

3. If a patient has HIV/TB co-infection and CD4 count is less than 100/ul, the continuation phase of TB treatment should consist of daily or three times weekly isonizaid and rifapentine. True or false?
   A. True
   B. False

4. The following statements are all true, except:
   A. MTD tests are assays used in the rapid identification of *M. tuberculosis*; results are obtained within two to seven hours after processing.
   B. Any individual who has a positive TST, with or without the presence of symptoms suggestive of TB, should have a chest radiograph.
   C. Persons with HIV/TB coinfection often present with typical findings on chest radiographs.
   D. Best practice is for patients to take anti-TB medications under directly observed therapy.

5. TB symptoms may include chronic cough, weight loss, fever, and night sweats. True or false?
   A. True
   B. False

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   Why or why not?

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