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IDCR and AAHIVM have united to improve the quality of health care delivery in the nation's correctional facilities by leveraging the knowledge, experience and resources of two diverse and accomplished groups of HIV and correctional health care experts.

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TB IN CORRECTIONS: CONSTANT COMPANION AND FUTURE SCOURGE

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Dislosures: ADG: Virco, Consultant, Speaker's Bureau; RR: Nothing to disclose

Introduction

Tuberculosis (TB) has recently regained attention in the international infectious disease news with the emergence of disease caused by highly drug-resistant strains of Mycobacterium tuberculosis in South Africa and the former Soviet Union. This highly resistant form of disease is called extensively drug resistant TB or "XDR TB" and is caused by isolates that have developed not only resistance to isoniazid and rifampin, but also to a fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin).[1]

The spread of TB and XDR TB is fueled by poor access to TB care, crowding, and the HIV epidemic.[2] In the former Soviet Union, a weakened public health system has contributed to the emergence and spread of resistant TB - especially in prison settings. The epidemics of injection drugs and TB have converged in Soviet prisons, a problem that is compounded by frequent interruptions of TB medication supply and antiquated approaches to care.[3]

Box 1. Definitions of MDR and XDR TB

MDR TB, or multidrug-resistant TB, is a specific form of drug-resistant TB. It occurs when the TB bacteria are resistant to at least isoniazid and rifampicin, two first line TB drugs.

XDR TB, or extensively drug-resistant TB is caused by an organism that in addition to being resistant to isoniazid and rifampin (MDR) also has resistance to any fluoroquinolone and at least one of three injectable second-line drugs (capreomycin, kanamycin, and amikacin).

While XDR TB is still not common (of 17,690 M. tuberculosis isolates obtained world-wide in 2003-2004, 20% were from patients with multidrug resistant (MDR) TB [i.e., resistant to isoniazid and rifampicin] and 2% were from patients with XDR TB) [1], the emergence of XDR TB in prison settings in the former Soviet Union, and the spread of XDR to the outside communities to which inmates and correctional officers belong, illustrates once again the important role that front-line professionals such as correctional health providers have to play in protecting the health of their charges and communities. This issue of *IDCR* will address a matter of perennial concern: TB treatment and prevention in correctional facilities.

XDR and MDR TB Prevalence

The emergence of resistance to anti-TB drugs is a phenomenon that occurs primarily due to poor TB control and inadequate management of TB disease. Problems include incorrect drug prescribing practices by providers, poor quality or erratic supply of drugs, and patient non-adherence.

XDR TB has been identified in all regions of the world but is most frequent in the countries of the former Soviet Union and in Asia. In the United States, 4% of MDR TB cases met the criteria for XDR TB. In Latvia, a country with one of the highest rates of MDR TB, 19% of MDR TB cases met the XDR TB criteria. Separate data on a recent outbreak of XDR TB in a population of HIV-infected patients in Kwazulu-Natal in South Africa was characterized by high mortality rates and deaths occurring within days to weeks after diagnosis. An investigation of this outbreak found that of the 544 TB patients studied, 221 had MDR TB; 47 out of the 544 patients and six health care workers were found to have XDR TB. Of the 53 subjects with XDR TB, 44 were found to have HIV infection, and 52 died, on average, within 25 days of XDR TB diagnosis, including those who were being treated with and responding to antiretroviral therapy.[4]

TB in the U.S.

In 2006, the prevalence of TB in the U.S. was 4.6 per 100,000 population. Although the TB case rates are much lower in the U.S. than rates elsewhere in the world, the rate of decline in TB prevalence has slowed in recent years, in part due to the persistence of TB among foreign-born populations and delayed diagnosis and treatment among members of racial and ethnic minority groups. Rates among American blacks, Asians and Hispanics were 8.4, 21.2, and 7.6 times higher than rates among whites, respectively. [5] The highest statewide TB case rate was 12.6 per 100,000, in Washington DC, (which is reported as a state in

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WHAT'S INSIDE

Letter from the Editor

Dear Correctional Colleagues,

As long as there have been humans, there has been tuberculosis. For millennia Mycobacterium tuberculosis has been shortening lives and today continues to ravage. Over a third of the population of our planet harbors the bacterium and an increasing subset is infected with drug resistant strains.

As with many of today's major infectious disease threats, human behavior has played a major role in fostering crisis. Indiscriminate use of anti-tuberculosis medications, suboptimal treatment adherence, cuts in the funding of successful tuberculosis (TB) control programs, global migration and the concentrating of persons at risk for the infection in medical and correctional facilities have each contributed to the resurgence in this infection; added to these is the companion epidemic of HIV.

Together these factors conspire within prisons and jails to create a 'perfect storm' in which the organism can be efficiently transmitted. Therefore, it is essential that correctional systems take seriously the threat posed by TB and implement policies and procedures to screen, diagnosis and treat those with the disease while limiting opportunities for the spread of the infection. Effective TB control programming requires knowledge, diligence and funding. We at *IDCR* cannot help with the last two but have dedicated this issue to the first in order to help increase understanding of TB for those working within jails and prisons.

IDCR Editor in Chief, Dr. Anne DeGroot and Dr. Renee Ridzon of the Bill and Melinda Gates Foundation have co-authored a comprehensive review of the major issues in the management and control of TB in correctional settings. A pair of case studies from Drs. Edward Gardner and Robert Belknap from Denver Public Health accompanies their article.

As we confront a world where multiple drug resistant TB is a frightening reality, it is essential we in corrections, of all people, not be lax when it comes to TB. The consequence of our failure would be dire and can be summed up vividly in one word: Russia.

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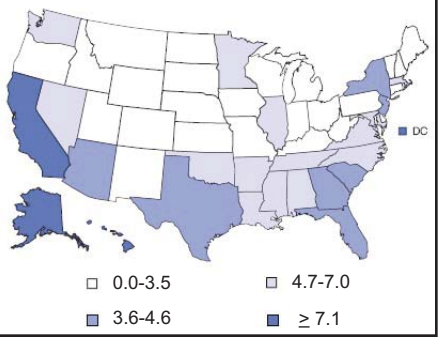
terms of U.S. TB surveillance). Seven states (CA, FL, GA, IL, NJ, NY and TX) reported more than 500 cases each - these states account for 60% of all TB cases.[5] (See Figure 1).

Figure 1. Rate* of tuberculosis cases, by state - United States. 2006 | *Per 100,000 population



Source: CDC. Trends in Tuberculosis Incidence United States, 2006. MMWR 2007;56(11):245-50

TB in U.S. Correctional Systems

While TB is on the decline in the U.S. and MDR TB rates are stable and low, both TB disease and latent TB infection (LTBI) are relatively prevalent inside U.S. prisons and jails. Reported TB case rates in federal and state prisons in 2003 were 29.4 and 24.2 cases per 100,000 inmates, respectively. These rates are considerably higher than the TB case rates reported for the non-inmate population in the U.S. reported for the same year (5.1 per 100,000 people).[6] The incidence of new cases of TB is also higher among inmates than non-incarcerated populations. In 1994 in New Jersey, the incidence of TB was 91.2 cases per 100,000 inmates, compared to a rate of 11.0 cases per 100,000 persons among all New Jersey residents. In 1991, a TB case rate for inmates of a California prison was 184 cases per 100,000 persons, which was 10 times greater than the statewide rate. In 2005, 16.5% and 10.5% of all reported TB cases in AZ and TX, respectively were in persons who were residents of correctional facilities.[7]

An investigation of TB cases in Memphis County demonstrates the significant role that correctional facilities play in the transmission and potential control of TB. This study examined the history of incarceration in all TB cases in the county and found that 43% of the TB cases reported in 1995 through 1997 were in persons who had previous contact with the jail. This suggests that the jail may have played an important part in contributing to the transmission of M. tuberculosis in the community as well as provided a potential location for prevention efforts in those who eventually developed cases of TB.[9]

Latent TB in correctional settings

The prevalence of LTBI seen among U.S. inmates can be as high as 25%. [10] A correlation has also been demonstrated between length of incarceration and positive tuberculin skin test (TST) response, indicating that transmission of M. tuberculosis is not uncommon in correctional facilities.[10] For this reason, jail and prison inmates, correctional officers and correctional health professionals are considered a "high risk group" that would benefit from annual TST screening, the best means to determine if there has been recent transmission of M. tuberculosis within a correctional facility (See Diagnostic Tests for TB, below).

Outbreaks in correctional settings

At least three factors contribute to the high rate of TB in correctional and detention facilities. First, incarceration leads to the concentration of individuals at high risk for TB (e.g., users of injected drugs, persons of low socioeconomic status, and persons with HIV infection) and who are unlikely to have received TB screening or treatment prior to incarceration. Second, crowded living conditions facilitate transmission. Third, the movement of inmates (without their medical records) from institution to institution, makes implementation of TB control measures difficult.

Reports of outbreaks of TB within U.S. prisons and jails are published on an almost annual basis.[11-17] In most of these outbreaks, epidemiology and strain typing verified transmission of a single strain of M. tuberculosis. Some of these outbreaks involved MDR strains; in several of these outbreaks, transmission occurred not only among inmates, but also to health care staff within the correctional facilities, and to members of the communities to which inmates were released. Several outbreaks that have been recently reported are summarized below:

Florida, 2001-2004. This outbreak of TB described in the February 2005 issue of *IDCR* illustrates the need for periodic screening of correctional staff members.[18] The outbreak investigation uncovered five cases of TB among correctional staff members that occurred over a period of two and a half years (May 2001-September 2004). The source case was an HIV-infected correctional staff member who was non-adherent with TB treatment. Restriction fragment length polymorphism, which is used to distinguish among strains of M. tuberculosis demonstrated that four of the five cases were caused by an identical strain, indicating a probable common source. Although mandatory screening and testing of all employees had been implemented three years prior to this outbreak, correctional staff members often did not comply. Additional prison-associated outbreaks have occurred in other regions of Florida; investigation of these outbreaks is ongoing.

Kansas, 2002. In Kansas, a single inmate with infectious TB had contact with more than 800 individuals as he was transferred from one jail (jail A) to two others (jails B and C) and eventually was remanded to a state prison. There was a lapse of 11 months between onset of symptoms and diagnosis. A contact investigation identified 318 of the possible 800 contacts; two were diagnosed with TB disease. Both were cellmates of the source case, one in jail A and the other in jail C. Isolates from all three patients had an identical-band RFLP. Of the 318 contacts, six with a prior documented negative skin test had a positive skin test and of 196 with no prior skin test information, 41 (21%) had a positive skin test.[19]

RFLP - restriction fragment-length polymorphism pattern- a molecular pattern that distinguishes one strain of TB from another.

South Carolina, 1999-2000. Segregating HIV-infected prisoners in a South Carolina prison contributed to a TB outbreak in which 71% of prisoners residing in the same housing area as the source case either had new tuberculin skin test conversion or developed TB disease. Thirty-one prisoners and one medical student in the community's hospital subsequently developed TB disease.[15]

Control of TB in Correctional Facilities

Control of TB in correctional facilities hinges on several important measures. First and most important is the rapid detection and proper treatment of potentially infectious cases of TB among inmates and staff. This is best accomplished with a proper index of suspicion for signs and symptoms of TB disease as well as adequate treatment and isolation of those with potentially infectious disease so that transmission of infection to others is minimized. Second is the prompt initiation of a contact investigation with case finding for additional cases of disease and those with recently acquired infection so that treatment can be administered. Third is initial and periodic screening (where indicated) so that those with undetected LTBI can be identified and treatment of infection can be initiated and completed, averting future cases of TB.

All suspect TB cases and clusters of new infections should be reported to the local TB control program and treatment of infection and disease should be conducted by those with experience in the management of TB or in consultation of those experienced in the management of TB. Health care providers with experience in the treatment of TB should manage all cases of infection and disease caused by drug resistant strains of M. tuberculosis. Apart from outbreaks of MDR TB in the U.S. in the late 1980s and early 1990s drug resistant TB in correctional facilities has not been a significant problem.[20,21]This has not been the case for the correctional systems of the former Soviet Union where a significant number of cases of drug resistant TB, including MDR TB have been and continue to be seen. To date the outbreak of XDR TB in South Africa is not known to involve prisoners, but the possibility exists for introduction to correctional facilities where, as has been shown in many circumstances, transmission may be enhanced. Because TB remains a problem in correctional facilities, the Centers for Disease Control and Prevention (CDC) has recently issued updated guidelines for the control of TB in these settings.[22] This latest set of guidelines focuses on case finding of persons (including inmates and staff) with potentially infectious pulmonary TB so that diagnosis and treatment (if indicated) can be promptly initiated to limit transmission of M. tuberculosis in the facility. The guideline outlines methods and timing that should be used to promptly screen inmates for TB disease in order to limit transmission within the facility. Recommendations for periodic screening are based both on the risk in individual inmates for TB and the risk of the facility as a whole. Below are some highlights from the CDC's 2006 Prevention and Control of Tuberculosis in Correctional and Detention Facilities guidelines (see reference for details on the recommendations outlined below).

Diagnostic Tests for TB

TST. The TST administered by injecting purified protein derivative (PPD) by the Mantoux method remains the most commonly used tool for the detection of infection with M.

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tuberculosis. In some persons with LTBI, reaction to tuberculin may wane over years.

When these persons are skin tested years after infection, they may have a negative reaction. However, the skin test may stimulate (or "boost") their ability to react to tuberculin, resulting in a positive reaction to a subsequent test. With serial testing, the boosted reaction may be misinterpreted as a newly acquired infection. Two-step testing is used to establish a reliable baseline TST status and reduce the likelihood that a boosted reaction will be misinterpreted as a recent infection because the second step of testing uncovers boosting. According to the updated guidelines, two-step testing should be used for initial testing in any individual (including staff and inmates) who has not had a TST in the prior 12 months. It should not need to be used for periodic testing unless there is a lapse of greater than 12 months between periodic tests and should never be used in the context of a contact investigation. The two-step test is performed by placing an initial TST, and if that test result is negative, then a second step TST should be done one to three weeks later. A positive reaction to the second-step test of the two-step test probably represents a boosted reaction. Although a boosted reaction should not be considered a TST conversion, it does indicate that that an evaluation for TB disease should be undertaken and if TB is not present, treatment for LTBI should be recommended if indicated.

A more accurate test?

In May 2005, the U.S. Food and Drug Administration licensed QuantiFERON®-TB Gold. (QFT-G). This in vitro test measures the amount of cytokine (interferon-gamma) produced by cells in whole blood that have been stimulated by peptides present in M. tuberculosis but absent from all BCG strains and from the majority of commonly encountered non-TB mycobacteria. The guideline outlines how this new test can be used for screening in correctional settings and points out that the test can be used as a diagnostic tool for M. tuberculosis infection, including both TB disease and LTBI. The utility of this test and the TST in those with advanced HIV disease and others with severe immunosuppression may be limited because of false negative test results and the use of QFT-G in the context of HIV infection is an area where continued research is needed. A negative TST or QFT-G in persons with severe immunosuppression should not be used as evidence to exclude the diagnosis of TB if there is presence of a reasonable index of suspicion of TB or signs and symptoms consistent with disease.

Neither the QFT-G nor the TST can distinguish between LTBI and TB disease; both tests must be used in conjunction with risk assessment, clinical history and examination, radiography, and other diagnostic evaluations. Limitations of QFT-G include that a blood specimen must be collected and processed within 12 hours of collection, that only a limited number of laboratories process the test, and that there is a lack of clinical experience in interpreting test results. Advantages of the test include fewer false positive tests from reactions from prior BCG or infection with environmental mycobacteria and elimination of the second visit for reading the TST. The elimination of a second visit will likely render the QFT-G competitive for a screening tool.

These new guidelines call for a classification of correctional settings by risk of TB among inmates, and how TB screening should be conducted is dependent on the classification of the facility as a minimal risk or non-minimal risk facility. A facility is classified as minimal risk if it meets all the following criteria:

- No cases of infectious TB have occurred in the facility in the last year;
- The facility does not house substantial numbers of inmates with risk factors for TB (e.g., HIV infection and injection drug use);
- The facility does not house substantial numbers of new immigrants (i.e., persons arriving in the U.S. within the previous five (years) from areas of the world with high rates of TB;
- Employees of the facility are not otherwise at risk for TB.

If these criteria are met, the facility should be classified as minimal risk. If not, it should be classified as non-minimal risk.

Regardless of type of facility, symptom screening for TB disease (including prolonged cough, weight loss, fever, night sweats) should be performed immediately on entry to a facility. Inmates who have symptoms suggestive of TB should be placed in an airborne infection isolation room and promptly evaluated for TB disease. If the facility does not have an airborne infection isolation room and there is a high suspicion of TB, the inmate should be transferred to a facility where he/she can be properly isolated so that a diagnostic evaluation can be conducted.[23]

For inmates in minimal risk facilities who have no symptoms of TB disease, only those with risk factors for LTBI or who are at increased risk of progressing from infection to disease should be screened within seven days of arrival with chest radiography or a TST or QFT-G. Risk factors that should trigger screening are shown in Box 2:

Box 2: Risk factors that should trigger screening for TB disease

- HIV infection (or suspicion of HIV infection)
- Recent immigration
- History of TB
- Recent close contact with a person with TB disease
- Injection-drug use
- Diabetes mellitus
- Immunosuppressive therapy
- Hematologic malignancy or lymphoma
- Chronic renal failure
- Medical conditions associated with substantial weight loss or malnutrition
- History of gastrectomy or jejunoileal bypass

Regardless of the TST or QFT-G result, inmates with known or suspected HIV infection or other severe immunosuppression should have a chest radiograph taken as part of the initial screening.

For those who are housed in non-minimal risk facilities, all inmates without symptoms should be screened with a TST, QFT-G (where available), or a chest radiograph should be performed within 7 days of arrival. HIV-infected inmates, those suspected of having HIV or those with immunocompromising conditions should have a chest radiograph regardless of TST or QFT-G result as part of the initial screening. The index of suspicion for TB in those with HIV infection should be very high as the presentation and radiographic appearance of TB in persons with advanced immunosuppression can be atypical.

Persons who have a positive TST or QFT-G result should be further evaluated for TB disease with a chest radiograph and symptom screen. The number of individuals who can effectively be screened in jail setting is limited because of the high rate of turnover and short lengths of stay.

In addition to screening for TB disease and for LTBI at entry, screening for LTBI should take place annually thereafter with either the TST or QFT-G in non-minimal risk settings and in those in minimal risk settings.

Protection of Staff

A medical history relating to TB should be obtained and recorded for all new employees upon hire, and a physical examination should be required. In addition, TST or QFT-G screening should be mandatory for employment. An annual TST or QFT-G should be performed for all employees with negative TST or QFT-G test.

Box 3. Diagnosis and treatment of LTBI

CDC Recommendations:

Regardless of age, correctional facility staff and inmates in the following high-risk groups should be given treatment for LTBI if their reaction to the TST is >5 mm or is the QFT-G is positive:

- HIV-infected persons
- Recent contacts of a TB patient
- Persons with fibrotic changes on chest radiograph consistent with previous TB disease
- Patients with organ transplants and other immuno-compromising condtions who receive the equivalent of >15 mg/day of prednisone for >1 month

Other inmates and staff

All other correctional facility staff and inmates should be considered for treatment of LTBI if their TST result is >10 mm induration or if the QFT-G is positive

Treatment

LTBI. The preferred treatment for LTBI is nine months of daily isoniazid or biweekly dosing administered by directly observed therapy (DOT). Individuals who have received BCG vaccine are still considered to have LTBI if their TST is positive (> 10mm). **(See Table 1)**

TB disease. In Spring 2003, the American Thoracic Society Infectious Diseases Society of America (IDSA), and the CDC issued updated guidelines for the treatment of TB.[1] These guidelines are substantially longer and significantly more comprehensive than the prior guidelines and should be referred to when treating a patient with TB disease or LTBI. The guidelines provide a complete discussion of the drugs currently available to treat TB, including dosing, dose adjustments needed for renal or hepatic dysfunction, toxicities, management of common adverse effects and information about interactions between antituberculosis drugs and other

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drugs. Because rifamycins have the potential for drug-drug interactions, including some antiretroviral medications, there is special attention given to the treatment of the patient with co-infection with HIV and M. tuberculosis **(See TB 101)**. There is discussion of treatment issues in special groups such as children and pregnant and breast-feeding women. Treatment completion is now determined by the number of doses delivered as well as the duration of therapy. Also included is an algorithm on how to manage treatment interruption, a problem that is not uncommon in correctional settings.

TB disease and LTBI should be treated by a provider experienced in the management of TB, or in consultation with an experienced clinician. All cases of suspected or confirmed TB disease should be promptly reported to the local TB control program and a contact investigation should be promptly initiated, if indicated. Cure of TB disease and successful treatment of infection depends on completion of the recommended course of therapy. Since the primary determinant of treatment outcome is adherence to the regimen, DOT is the preferred treatment strategy. DOT should be used throughout the entire course of therapy. In the case of intermittent treatment regimens for LTBI, nonadherence to dosing results in a larger proportion of total doses missed than daily dosing; therefore, all patients on intermittent treatment should also receive DOT. DOT should also be used with daily dosing of LTBI treatment whenever feasible. Practitioners providing treatment to inmates should coordinate DOT with the local health department on an inmate's release.

DOT implementation in corrections can require a rigorous approach. The first order of business is the crafting of reliable inmate/patient logs, which may be paper or electronic. These should generate daily listings of all DOT inmate/patients to receive medication that day. In concert with security, recall systems are required in order to track down and bring to the clinic all "No-Shows" for receipt of DOT. This may entail tracking down not only voluntary "No-Shows", but also the few cases that be unavailable to receive medicine, such as detainees/inmates who may have been in court that day, or were temporarily absent for a variety of reasons. Finally, with inmates waiting for DOT security cooperation in the form of a Deputy or correctional officer will be needed. Once medication is administered, there should be assurance that it has been swallowed. This can be done by shining a flashlight into the inmate/patient's throat after medication is given. On the inside of prison walls, as is also often true on the outside, patients are likely to be more adherent if they are well educated about their disease.

Conclusions

Correctional facilities are not closed institutions and are a part of the surrounding community. Good public health practices inside will lead to improved public health outside. Movement between the facility and the community occurs through the arrival and departure of inmates, staff and visitors. Because of this movement, poor TB control within correctional facilities will eventually result in problems with TB control outside of these facilities. Conversely, good TB control practices within correctional facilities will translate to better TB control within correctional facilities as well as the surrounding communities. Correctional facilities house and congregate members of vulnerable populations who are at high risk for TB. While this creates a situation where undetected TB can spread easily, it also presents an opportunity to provide interventions for detecting and treating TB disease and LTBI among a high risk population, resulting in an overall benefit to the inmates and society and a means to strive toward the goal of TB elimination in the U.S.

Table 1. Drug Regimens for the Treatment of LTBI

Drugs	Duration (mo)	Interval	Minimum # Doses
Isoniazid	9	Daily Twice Weekly	270 doses 76 doses
Isoniazid	6	Daily Twice Weekly	180 doses 52 doses
Rifampin	4	Daily	120 doses
Rifampin/Pyrazinamide	Generally should not be offered for treatment of LTBI*		

Source: CDC. Treatment of Latent Tuberculosis Infection. 2006:2.
** CDC. Update: Adverse Event Data and Revised American Thoracic Society |CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection. MMWR | 2003; 52 (No.31). http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm*

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Case Studies in the Treatment of Tuberculosis in the Correctional Setting

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Disclosures: Nothing to disclose

Case 1:

A 28 year-old male was brought to a jail medical facility after being arrested for assault. He was intoxicated and complained of chest pain, cough, and night sweats intermittently for several weeks prompting the Sheriff's Deputy to alert the facility nurse. He had no significant past medical history, was born in Mexico and had been living in the United States for the past three years. His vital signs and physical exam were normal except for a heart rate of 120 beats per minute. A chest radiograph showed a faint left upper lobe fibronodular opacity. Based on his presentation the patient was placed in respiratory isolation. What should you do next?

Discussion:

Diagnosing tuberculosis (TB) is challenging because the symptoms are often nonspecific and varied. The critical first step involves considering TB in the differential diagnosis for a broad range of symptoms. Approximately half of all TB cases admitted to the hospital have a delay in diagnosis primarily because TB is not initially considered.[1,2]

The next step is to evaluate the patient's risk factors for 1) latent TB infection and 2) TB disease. In the U.S., the most common risk factor for infection is birth or residence in a high prevalence country (essentially anywhere other than North America, Western Europe, Australia or New Zealand). Other risks for infection include work or residence in a correctional facility, nursing home, or other congregate setting, current or prior homelessness, and substance abuse. Common risks for progression to TB disease include HIV-infection, other immunosuppressive illnesses or medications, diabetes, chronic renal failure, and scarring from prior TB on chest radiograph.

All suspect patients should have a chest radiograph performed. Remember that the chest radiograph cannot always differentiate between active TB and old scarring. Once TB is suspected, the patient should be placed in respiratory isolation until it is determined if the patient has infectious pulmonary TB or an alternative diagnosis is made. All suspected or confirmed TB cases should be promptly reported to the department of health. In correctional settings without availability of airborne infection isolation rooms, evaluation of suspect cases may require hospital admission.

Along with the chest radiograph, assessment for active TB involves collecting three sputum smears and cultures, and placing a tuberculin skin test (TST) or performing a quantiferon test. These screening tools are helpful when positive by confirming that the patient was infected with M. tuberculosis at some time in their life. Alone the TST or quantiferon test cannot distinguish between TB disease and latent TB infection. Both of these tests can produce false negative results in as many as 25% of people with TB disease.[3]

Sputum smears and cultures are an important part of an initial evaluation for pulmonary TB. Traditionally, sputum samples have been collected on three successive mornings but some have suggested samples collected 8 hours apart with at least one early morning specimen may be adequate and shorten the time needed to collect these diagnostic tests.[4,5] Unfortunately, sputum smears have a poor sensitivity with only 50% of patients with pulmonary TB having a positive smear.[3]

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While smear positive TB patients are the most infectious, patients who have smear negative pulmonary disease can also transmit M. tuberculosis.[6] All suspect cases need to be followed closely while waiting for culture results and if released from incarceration, should be referred to the local health department for appropriate follow up.

In this case, the patient had a negative TST and three negative sputum smears. He was discharged from the hospital on azithromycin and released on bail. Three weeks later, cultures of all three sputum specimens were positive. His only contact information turned out to be a center for alcohol treatment where he hadn't been since his arrest. This highlights the importance of collecting extensive contact information from patients, such as this one, who had suspected TB. Information about family members and friends who may know where the patient is located can be obtained from the patient prior to release. In addition, reporting the suspected case to the local department of health, in accordance with local procedures, can be an important element in post-release follow-up. This patient was finally found a month later when he returned to the treatment center and learned the TB clinic was looking for him. He had an HIV antibody test performed and this was negative.

He was started on four-drug TB therapy until drug sensitivities were able to be completed. A repeat TST while on treatment was strongly positive which is not uncommon. Two months later his organism was found to be sensitive to isoniazid and rifampin, his remaining treatment was simplified to these antibiotics, and he was continued on directly observed therapy.

Case 2:

A 29 year-old Hispanic male was referred to the hospital from the state prison with postprandial abdominal pain for several months that had acutely worsened over the past week and was associated with nausea, vomiting and fevers. He was born in Honduras, had lived in the U.S. for 10 years and had been incarcerated for six months. An ultrasound showed a thickened gall bladder and dilated extra-hepatic biliary ducts. He was diagnosed with cholecystitis and initially treated with intravenous levofloxacin and metronidazole. He improved clinically and was discharged to the prison infirmary on intravenous ticarcillin/clavulanate, but returned to the hospital three days later for increasing pain and fevers. What should you do next?

Discussion:

During the initial infection with TB, the bacilli replicate in the alveoli, enter the lymphatics and bloodstream, and disseminate throughout the body. For most people, the immune system contains the infection through the formation of granulomas. Only about 5-10% of persons infected will progress to active TB during their lifetime with 80 - 85% of these patients having pulmonary TB and 15 - 20% having extrapulmonary TB.[3]

The most common extrapulmonary sites in descending order of frequency are lymphatic, pleural, bone and joint, meningeal, peritoneal, genitourinary, and then other sites.[3] The presenting signs and symptoms depend on the location of disease but may include more typical symptoms such as fever, night sweats, and weight loss. Importantly, some patients presenting with extrapulmonary symptoms will have active pulmonary TB as well. The occurrence of active disease at multiple sites is more common in immunocompromised patients, particularly those with advanced HIV infection. All patients being evaluated for extrapulmonary TB should have a chest radiograph due to the risk for occult pulmonary TB with the potential for airborne transmission to others.

While diagnosing pulmonary TB can be challenging (Case 1), diagnosing extrapulmonary disease can be even more difficult. As with pulmonary TB, the key to a timely diagnosis requires consideration of TB in the differential diagnosis. Many sites, like pleural, peritoneal, meningeal, and pericardial, are associated with a very low organism burden. Therefore, smears are rarely positive and cultures of fluid are less than 50% sensitive. Nucleic acid amplification tests were developed in part to address this limitation and are highly specific but unfortunately lack sufficient sensitivity to assume a negative test excludes the diagnosis.[7] Therefore, definitive diagnosis of extrapulmonary TB often requires a tissue sample for pathology and culture.

Delays in diagnosis of pulmonary and extrapulmonary TB can be increased by the empiric use of fluoroquinolones. Many fluoroquinolones are active against Mycobacterium tuberculosis and some are under investigation as first line agents in combination therapy.[8,9] Because patients can have a profound clinical response, clinicians may be fooled into a false sense of security since treatment with fluoroquinolones can temporarily lead to suppression of organism growth in cultures. As with any other single agent, treatment with a fluoroquinolone will not cure TB, and patients will relapse, often soon after stopping therapy.

Continued on page 7

COVERAGE OF THE 14TH CONFERENCE...
(continued from page 5)

In our patient, a biliary drain was placed for symptom relief and plans made for surgical exploration. Prior to surgery, samples of his biliary fluid and stool were sent to microbiology, where an AFB smear was positive, and eventually grew M. tuberculosis. His clinical response during the first hospitalization was thought to be from the levofloxacin he received, but his symptoms quickly returned when he was switched to an antibiotic without activity against M. tuberculosis. He was started on standard four drug TB therapy with isoniazid, rifampin, pyrazinamide, and ethambutol. An HIV test was performed and was positive. The patient's CD4 cell count was 237/mm_3 and it was decided to defer initiation of HIV therapy for approximately three to six months when there may be reduced risk of immune reconstitution reaction. When concomitantly administered, HIV and anti-tuberculous therapy have to be carefully selected to avoid drug-drug interactions (see *IDCR* February 2006 and this issue's TB 101 for a detailed discussion of antiretroviral and TB drug interactions).

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RESOURCES

CDC. Prevention and Control of Tuberculosis in Correctional and Detention Facilities: Recommendations from CDC. MMWR 2006;55(No.RR-9).
www.cdc.gov/mmwr/pdf/rr/rr5509.pdf

CDC's 2003 Recommendations for the Treatment of Tuberculosis
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

CDC's Division of Tuberculosis Elimination
http://www.cdc.gov/tb/

Slides from the NCCHC Pre-conference Seminar
Infectious Diseases in Corrections: An Expert Panel
October 28, 2006
http://www.idcronline.org/archives.html

Department of Health and Human Services
2006 Adult and Adolescent Antiretroviral Treatment Guidelines
http://www.aidsinfo.nih.gov/guidelines/

International AIDS Society-USA Panel
2006 Recommendations of the Treatment for Adult HIV Infection
http://jama.ama-assn.org/cgi/content/full/296/7/827

CDC's Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm

American Academy of HIV Medicine
http://www.aahivm.org/

To watch a CME-accredited web-stream of "Occupational & Non-Occupational Post-Exposure Prophylaxis"
www.amc.edu/hivconference

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TB101: RIFAMYCIN DOSING IN TB/HIV CO-INFECTION

Rifamycin Dosing in TB/HIV Co-infection Non-Nucleoside Reverse Transcriptase Inhibitors

	Efavirenz (EFV)	Delavirdine (DLV)	Nevirapine (NVP)
Rifampin	Consider increasing EFV to 800 mg QHS No change necessary for Rifampin Levels: EFV decreased by 25%	Contraindicated Levels: DLV decreased by 95%	Not recommended Levels: NVP decreased by 37-58% Note: If alternative therapy not available, administer standard doses of NVP and Rifampin and monitor antiviral response and liver function tests closely as combination may increase risk of hepatotoxicity
Rifabutin	Increase Rifabutin to 450 mg daily No dosing change necessary for EFV Levels: Rifabutin decreased by 35%	Contraindicated Levels: DLV decreased by 80%	No dosing change necessary for Rifabutin or NVP Levels: NVP decreased by 16%

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TB101: Rifamycin Dosing in TB/HIV Co-infection *(Cont.)*

Rifamycin Dosing in TB/HIV Co-infection Protease Inhibitors

	Indinavir (IDV)	Ritonavir Full dose (RTV)	Saquinavir (SQV)	Nelfinavir (NFV)	Fosamprenavir (f-APV)	Atazanavir (ATV)	Lopinavir* (LPV)	Tipranavir* (TPV)
Rifabutin	If NOT RTV boosted: Decrease Rifabutin to 150 mg daily or 300 mg 3x/week; Increase IDV to 1000 mg every 8 hours Levels: Rifabutin increased by 2-fold IDV decrease by 32% If RTV boosted: Decrease Rifabutin 150 mg QOD or 150 mg 3x/week; No IDV dose adjustments are necessary Levels: No Data	Decrease rifabutin to 150 mg QOD or dose 3x/week. Levels: Rifabutin concentrations increase 4-fold.	If NOT boosted: Contraindicated If RTV boosted: Decrease Rifabutin 150 mg QOD or 150 mg 3x/week. No SQV dose adjustments are necessary Levels: No Data	With NFV 1250 mg Q12H decrease Rifabutin to 150 mg QD or 300 mg 3x/week. No NFV dose adjustments are necessary Levels: No Data	If RTV NOT concomitantly administered: Decrease Rifabutin to 150 mg QD or 300 mg 3x/week. No f-APV dose adjustments are necessary Levels: Rifabutin increased 1.9-fold If RTV boosted: Decrease Rifabutin to 150 mg QOD or 3x/week. Levels: Rifabutin increased	Decrease Rifabutin dose to 150 mg QOD or 3x/week No ATV dose adjustments are necessary Levels: Rifabutin increased 2.5-fold	Decrease Rifabutin dose to 150 mg QOD or 3x/week. No dose adjustments are necessary for LPV/r Levels: Rifabutin increased 3-fold.	Decrease Rifabutin to 150 mg QOD or 3x/week. Levels: Rifabutin increased 2.9-fold.
Rifampin	Contraindicated Levels: IDV (unboosted) decreased 89% IDV (boosted) decreased 87%	Alternate antimicrobial should be considered. Levels: RTV decreased by 35%. .	Contraindicated Levels: SQV levels decreased by 84%. Note: Severe hepatotoxicity observed with Saquinavir 1000 mg/RTV 100 mg Q12 hours + Rifampin 600 mg daily	Contraindicated Levels: NFV decreased by 82%	Contraindicated Levels: APV decreased by 82%;	Contraindicated Levels: No data	Contraindicated Levels: LPV decreased by75% Limited clinical experience suggests LPV/r 3 SGC + RTV 300 mg BID may overcome interaction. Hepatotoxicity may be associated with increase RTV dose. Rifabutin is recommended instead of Rifampin	No data Should NOT be co-administered

*By: Todd Correll. PharmD, BCPS and Nichole Kiziah**, PharmD*

Disclosures: *TC: Consultant: Pfizer, Speaker's Bureau: Gilead Sciences, Abbott Laboratories; NK: Speaker's Bureau: Gilead, Boehringer-Ingelheim*
NK: Assumes ATV, LPV and TPV boosted with RTV

Notes:
NRTIs not expected to have clinically significant interactions with rifamycins. For patients with CD4 cell counts <100 cells/mm3, daily or three times weekly TB regimens are preferred. If patients are not receiving NNRTI- or PI-based antiretroviral therapy, Rifampin can be used in place of Rifabutin. If a three times weekly TB regimen is preferred, Rifabutin does not require dose alteration when concomitantly administered with a RTV boosted PI-based antiretroviral regimen (i.e. if on ATZ/RTV the Rifabutin dose would be 150 mg every other day or three times per week). Please see recommendation in above table for Rifabutin dosing recommendations when co-administered with a PI.
If an Efavirenz-based regimen is used, Rifabutin 600 mg three times weekly is recommended.
INH, PZA and EMB require escalation in doses if a three times weekly regimen is preferred.

IDCR-O-GRAM

Figure 1 - TB Screening: Minimal Risk Facility

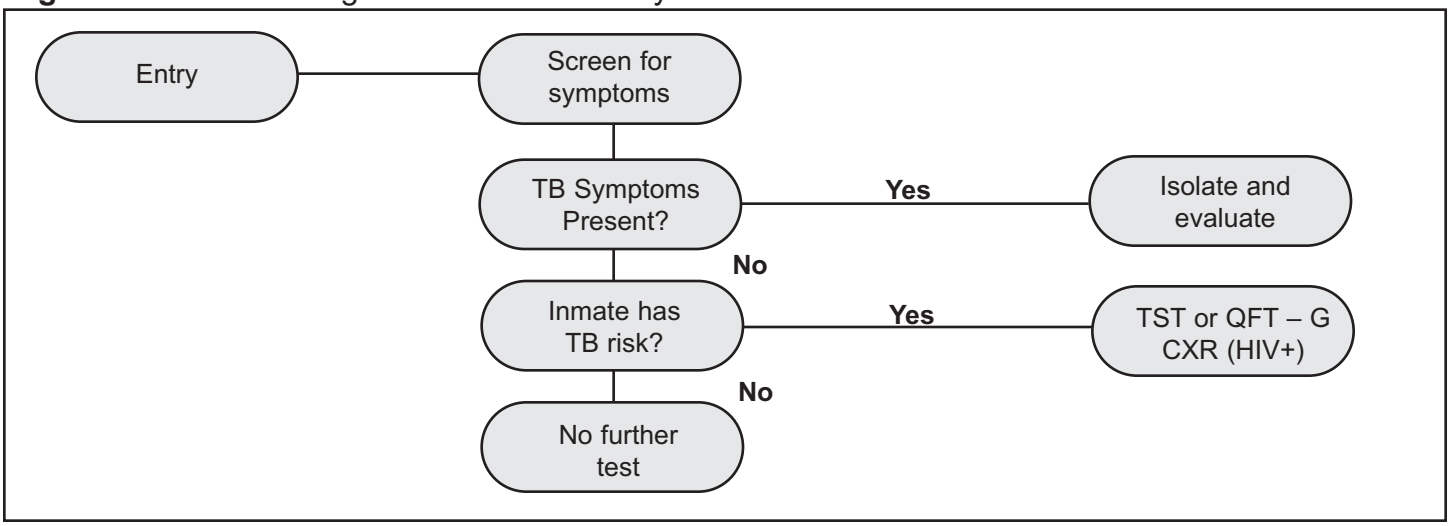


Figure 2 - > TB Screening: Minimal Risk Facility

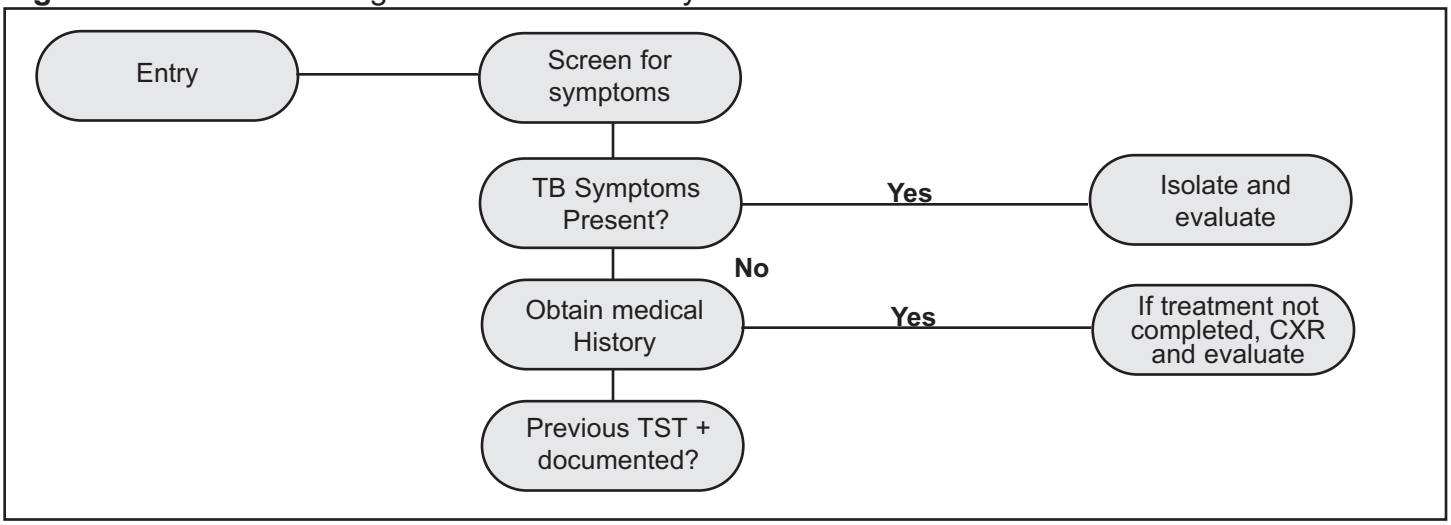
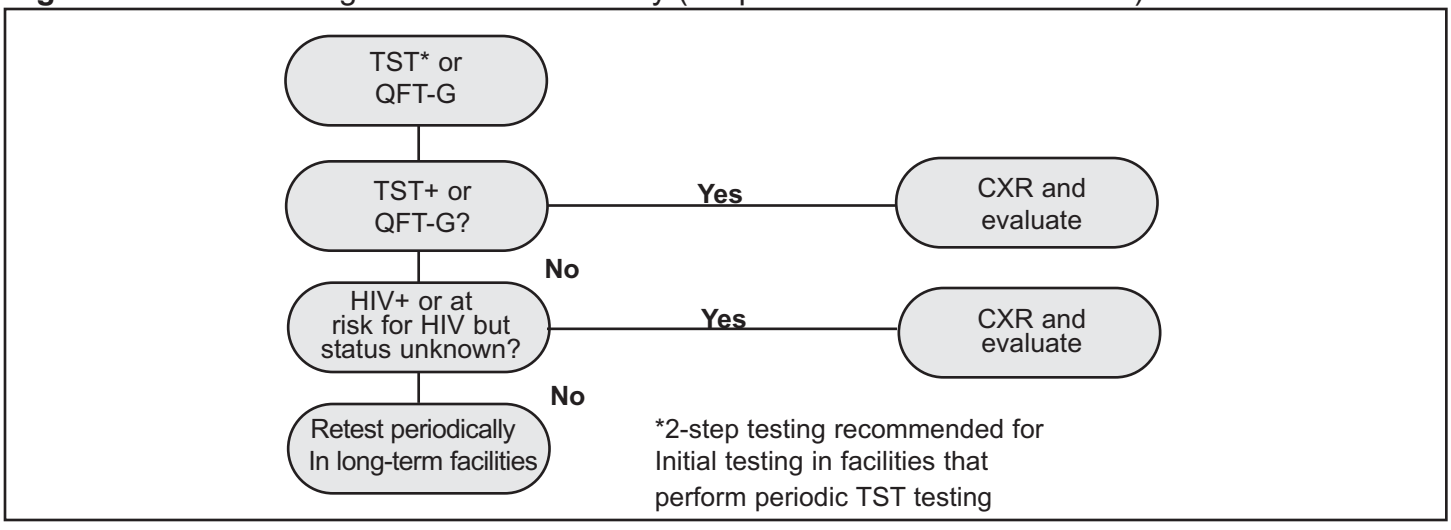


Figure 3 - TB Screening: Minimal Risk Facility (No previous TST+ documented)



Source: *Prevention and Control of Tuberculosis in Correctional and Detention Facilities: Recommendations from CDC. MMWR 2006;55(RR-9)*

Save the Dates

Medication Assisted Therapy (MAT): Interventions for Drug Users in Correctional Settings
American Correctional Health Services Association (ACHSA) 2007 Multidisciplinary Professional Development Conference
June 4, 2007
Reno, NV
Visit:http://www.achsa.org/display-common.cfm?an=1&subarticlenbr=49

Dual Focus on Correctional Health: Legal and Ethical Considerations and Emerging Issues
American Correctional Health Services Association (ACHSA) 2007 Multidisciplinary Professional Development Conference
June 5-7, 2007
Reno, NV
Visit:http://www.achsa.org/display-common.cfm?an=4

Correctional Mental Health Seminar
Las Vegas, NV
July 15-16, 2007
Visit:www.ncchc.org/education/MH2007/lasvegas.html

IAS 2007: 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention
Sydney, Australia
July 22-27, 2007
Visit:www.ias2007.org/start.aspx

47th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC™)
Sydney, Australia
July 22-27, 2007
Visit:www.icaac.org

National Conference on Correctional Health Care
Nashville, TN
October 13-17
Visit:http://www.ncchc.org/education/national2007.html

News and Literature Reviews

Pattern of US Tuberculosis Cases Shifting

Utilizing data from a recent study of tuberculosis (TB) cases among foreign-born persons in the United States, this news article, published in the Journal of the American Medical Association, highlights the changing epidemiological trends in tuberculosis (TB) cases in the United States.[1] Despite the fact that TB cases among US-born residents between 1993 and 2004 fell by 62%, cases among foreign-born residents rose by 5% during the same time period, growing from 29% to 54% of total cases. Notably, of all the reported cases among foreign-born residents in 2004, about half had lived in the United States for at least five years. The increasing proportion of cases among foreign-born individuals who have lived in the United States for more than five years renders existing recommendations, which call for tuberculin skin testing and treatment of latent infections only among those who have lived in the United States for less than five years, obsolete. While new guidelines are under review, many experts, the article suggests, fear that rising cases in immigrant populations together with cutbacks in state and federal TB-control programs could create a resurgence in TB cases, similar to that seen in the United States in the late 1980s and early 1990s.

1. Tuberculosis among foreign-born persons in the United States: achieving tuberculosis elimination. Cain, KP et al. American Journal of Respiratory Critical Care Medicine. 2007; 175:75-79.

Pattern of US Tuberculosis Cases Shifting. Voelker, R. Journal of the American Medical Association. 2007 Feb;297(7): 685.

Missed Opportunities for Earlier Diagnosis of HIV Infection - South Carolina, 1997-2005

In this study, originally published in *MMWR*, investigators examined opportunities to detect HIV infection among all cases of HIV and AIDS reported in South Carolina prior to the 2006 release of revised CDC guidelines for HIV testing in health-care settings. Of the 4,315 reported cases of HIV infection from 2001-2005, 41% were late-testers, defined as persons in whom AIDS was diagnosed within one year of the initial HIV diagnosis. By linking data from the South Carolina HIV/AIDS Reporting System (HARS) and the South Carolina Office of Research and Statistics (ORS), the investigators were able to determine that 73% of the late-testers had made at least one documented visit to a South Carolina health-care facility between 1997 and 2005. In total, these late-testers made 7,988 visits to various facilities such as emergency departments (79.9%), inpatient settings (12.3%), outpatient facilities (7.4%), and free clinics (1.4%). 79% of the resulting diagnoses were categorized as not likely to be suggestive of an HIV infection, even though 33.9% of the late-testers were identified as persons with high risk practices that should have prompted HIV screening if risk histories had been elicited. These findings, the authors assert, suggest that routine, opt-out HIV screening of all patients, rather than risk based testing, might result in substantially earlier HIV diagnoses in South Carolina.

In an accompanying editorial, authors from the CDC note that the findings from the South Carolina study support the new recommendations for routine, opt-out HIV screening in all health care settings. Additionally, they highlight the fact that a substantial proportion of the newly diagnosed HIV cases in 2004-2005 had low CD4+ cell counts, suggesting a high prevalence and long duration of undiagnosed HIV infections in South Carolina. In considering the limitations of the report, the members of the CDC point out that certain HIV/AIDS diagnoses may not have been reported to HARS/ORS, the matching of records might not have been successful in all cases, patients might have rejected HIV testing, and certain late-testers may not have been HIV infected during the time of their health care visits. In conclusion, they remark that the capacity of treatment and preventive services in South Carolina will need to increase if HIV testing is made routine.

Missed Opportunities for Earlier Diagnosis of HIV Infection - South Carolina, 1997-2005. Duffus W. et al. Journal of the American Medical Association. 2007;297(2):149-150.

Reducing Tuberculosis Incidence by Tuberculin Skin Testing, Preventive Treatment, and Antiretroviral Therapy in an Area of Low Tuberculosis Transmission

Researchers in Switzerland, an area with low rates of TB transmission, assessed the effect of tuberculin skin testing (TST) and preventive treatment on the incidence of tuberculosis (TB). Using data from the more than six thousand participants in the Swiss HIV Cohort Study (SHCS), the investigators calculated a TB incidence of 0.22 cases per 100 person-years in the overall study population. Among the 69% of individuals who received TST, 9.4% had positive results. Significantly, if preventive treatment was not administered, the incidence of TB was found to be 1.6 cases per 100 person-years in those patients with positive TST results. In contrast, none of the 193 TST positive patients who received preventive treatment developed TB. Increased risk for TB in the study population included: positive TST results, missing TST results, origin from sub-Saharan Africa, low CD4+ cell counts, and high plasma HIV RNA levels. Those patients receiving combination antiretroviral therapy were at a reduced risk. The authors suggest that potential study limitations include an underestimation of TB incidence due to the short follow-up period of two years and possible delay between the diagnosis of HIV or TB and registration in SHCS. Nonetheless, the investigators conclude that screening for latent TB using TST and preventive treatment for patients with positive TST results remains an efficacious strategy for reducing TB-associated morbidity in a country with low rates of TB transmission.

Reducing Tuberculosis Incidence by Tuberculin Skin Testing, Preventive Treatment, and Antiretroviral Therapy in an Area of Low Tuberculosis Transmission. Elzi, L et al. Clinical Infectious Diseases. 2007 Feb;44: 94-102.

Compiled by Ross Boyce, MS2

Self-Assessment Test for Continuing Medical Education Credit

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for continuing Medical Education through the joint sponsorship of Medical Education Collaborative, Inc. (MEC) and *IDCR*. MEC is accredited by the ACCME to provide continuing medical education for physicians.

Medical Education Collaborative designates this educational activity for a maximum of 1.5 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity. Statements of credit will be mailed within 6 to 8 weeks following the program.

Objectives:

- The learner will be able to describe the appropriate usages of DOT when treating TB.
- The learner will be able to describe the factors that contribute to the high rates of TB infection in correctional facilities.
- The learner will become familiar with the recommended TB screening methods and procedures.

1. True or False? DOT should be used for the treatment of TB disease, intermittent treatment regimens for LTBI, and daily dosing treatment regimen of LTBI?

   TRUE or FALSE?

2. Which of the following is NOT a factor that contributes to the high rate of TB infection in correction and detention facilities?

   A. The movement of inmates (without their medical records) from institution to institution.
   B. The concentration of individuals at high risk for TB (e.g., users of injected drugs, persons of low socio- economic status, and persons with HIV infection).
   C. The physical structure of correctional facilities that are in many cases overcrowded.
   D. All of the above

3. True or False? Two-step testing should be used for periodic testing unless there is a lapse of greater than 12 months between periodic tests and should be used in the context of a contact investigation.

   TRUE or FALSE?

4. All are limitations of QuantiFERON®-TB Gold. (QFT-G) EXCEPT:

   A. Only a limited number of laboratories process the test.
   B. Blood specimen must be collected and processed within 12 hours of collection.
   C. The rate of false positives in non-immnosuprressed patients.
   D. There is a lack of clinical experience in interpreting test results.

5. Which of the following is not a factor that should prompt TB screening:

   A. History of tobacco use
   B. Chronic renal failure
   C. Hematologic malignancy or lymphoma
   D. Immunosuppressive therapy

6. Which of the following statements regarding sputum smears is correct:

   A. They have a poor sensitivity with only 50% of patients with active pulmonary TB having a positive smear
   B. Patients who have smear negative disease can also transmit the infection
   C. A single negative smear is sufficient to rule out active disease
   D. A and B
   E. A, B and C

In order to receive credit, participants must score at least a 70% on the post test and submit it along with the credit application and evaluation form to the address/fax number indicated. Statements of credit will be mailed within 6-8 weeks following the program.

Instructions:

- Applications for credit will be accepted until May 31, 2008.
- Late applications will not be accepted.
- Please anticipate 6-8 weeks to recieve your certificate.

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Please check which credit you are requesting ___ ACCME or ___ Non Physicians

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COURSE EVALUATION

I. Please evaluate this educational activity by checking the appropriate box:

Activity Evaluation					
	Excellent	***Very Good***	***Good***	***Fair***	***Poor***
Faculty					
Content					
How well did this activity avoid commercial bias and present content that was fair and balanced?					
What is the likelihood you will change the way you practice based on what you learned in this activity?					
Overall, how would you rate this activity?					

II. Course Objectives

Were the following overall course objectives met? At the conclusion of this presentation, are you able to:

- The learner will be able to describe the appropriate usages of DOT when treating TB. **YES** **NO** **SOMEWHAT**
- The learner will be able to describe the factors that contribute to the high rates of TB infection in correctional facilities. **YES** **NO** **SOMEWHAT**
- The learner will become familiar with the recommended TB screening methods and procedures. **YES** **NO** **SOMEWHAT**

III. Additional Questions

a. Suggested topics and/or speakers you would like for future activities.

b. Additional Comments