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Infectious Diseases in Corrections

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INFECTIOUS DISEASES IN CORRECTIONS REPORT

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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).

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TUBERCULOSIS IN CORRECTIONS

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***DISCLOSURES:** *; **Nothing to disclose*

Tuberculosis (TB) continues to disproportionately afflict persons incarcerated in correctional facilities in the United States (U.S.). A recent study examining surveillance data for all persons with TB disease reported in the U.S. between 1993 and 2003 found that the rate of TB disease among federal (29.4 cases/100,000) and state (24.2/100,000) prison inmates was markedly higher than the rate among non-inmates (6.7/100,000) (see Literature Review).[1] Over half (53.7%) of the inmates with TB disease were housed in local jails, and compared to non-inmates, they were younger, more likely to be male, US-born and from racial and ethnic minorities. Not surprisingly, inmates more often had a history of excess alcohol use, illicit drug use and homelessness during the year prior to TB diagnosis. Co-infection with human immunodeficiency virus (HIV) was common among inmates with TB disease. Among males between the ages of 18 and 64, 25% of the incarcerated were known to be HIV-infected compared to 18% for non-inmates. Further, despite a higher rate of directly observed therapy among inmates than non-inmates, treatment completion rates tended to be worse among inmates than non-inmates, particularly among those who were HIV-infected.

As most prisoners with TB are eventually released, failure to complete treatment in this population poses a significant risk not only to the individual health of the patient, but also to the public health of the community. While the study did not examine the reasons for worse TB treatment outcomes among inmates, several factors may have been contributory. The study spanned 1993 to 2003, and during the early part of this period, TB control efforts were simultaneously recovering from the relative neglect of the previous decade and coping with the emerging HIV/AIDS epidemic. Additionally, the authors suggest that the poor inmate outcomes observed may be the product of fragmentation of care in correctional settings due to inmate transfer between institutions and release from incarceration, which challenge coordinated care to ensure treatment completion. Certainly, socioeconomic factors associated with incarceration may have posed a barrier to healthcare as those who are incarcerated may have less access to care and/or under-utilize care.

Local jails have been particularly implicated in TB transmission, and TB control has been challenging in this setting. A study of TB cases in

Continued on page 2

WHAT'S INSIDE

Tuberculosis in Corrections
(continued from page 1)

Maricopa County, Arizona, published in 2005, demonstrated the challenges of TB control in jails.[2] Of 300 TB cases reported in the county from 1999 to 2000, 73 (24%) occurred in persons who had a history of incarceration in the county jail. Similar to national statistics, TB patients with a history of incarceration had higher rates of homelessness and substance abuse than other TB patients. The TB patients in the study who had been in the county jail were incarcerated a total of 370 times, but spent a median of only two days in jail each time they were incarcerated. This short length of stay and the requirement of at least 48 hours to place and read a tuberculin skin test (TST) may explain why 83% of inmates had no record of tuberculin skin testing in jail. Innovative strategies for screening (e.g. Quantiferon-Gold®, see below) and enhanced follow-up after incarceration are needed to target this high-risk population.

Occupational Hazard of TB Infection among Healthcare Workers in Prisons and Jails

TB is an occupational hazard for healthcare professionals who work in correctional settings. Past studies have demonstrated a relatively high incidence of latent TB infection (LTBI) in correctional healthcare workers,[3] with infection rates estimated to be as high as 6.6%.[4] However, a recent study of correctional healthcare workers suggested that a significant proportion of LTBI may be acquired outside the workplace.[5] The study authors surveyed correctional healthcare professionals in Rhode Island, Maryland and Texas. Tuberculin skin testing practices varied by site, and two-step testing (i.e. repeat tuberculin skin testing one to three weeks following an initial negative TST result) was generally not used. The prevalence of LTBI was 18%, with an estimated infection rate of 1.3%/year. The risk of TB infection correlated with birth in a high-incidence country, but not with job title, duration of employment or TB screening practices in the workplace.

The results of this study reinforce the importance of TB screening among correctional healthcare staff at the time of hire and the use of the two-step testing procedure to distinguish prior TB infection from infection acquired in the workplace Persons with remote TB infection may have a negative TST on initial testing, but placement of the TST stimulates the immune system, which may cause the next TST to be positive in a previously infected person. If the next TST is placed one to three weeks later, it is unlikely that a new exposure to TB has occurred; a positive TST likely represents a boosting of the immune response and not new infection. If two-step testing is not performed, a positive TST during screening the following year will be interpreted as recent TB infection when in fact it may represent immune boosting. Continued refinement of TB surveillance strategies will be necessary to accurately detect ongoing TB transmission in the high-risk correctional environment.

To assist in protecting healthcare workers, in December 2005 Centers for Disease Control and Prevention (CDC) released "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005."[6] The document divides healthcare facilities into low risk, medium risk and potential ongoing transmission settings, based on the number of patients with TB disease seen at the facility. The recommended frequency of healthcare worker TST screening varies depending on the facility risk level. Correctional healthcare facilities are classified as medium risk unless ongoing TB transmission is identified and all correctional healthcare facilities should have a written TB infection control plan.

In medium risk settings, all healthcare workers should receive baseline TB screening upon hire (either with two-step tuberculin skin testing or a single interferon-γ release assay, e.g. QuantiFERON®). After baseline testing, healthcare workers should receive TB screening annually, including screening for symptoms and either tuberculin skin testing or interferon-γ release assay for persons with previously negative tests. Healthcare workers with a positive baseline test, a newly positive test or documentation of previous treatment for latent or TB disease should receive one chest radiograph to exclude TB disease. Yearly chest radiographs are not needed unless TB symptoms are present. In the setting of ongoing transmission within a facility, TB testing may need to be performed as frequently as every eight to 10 weeks until there is no further evidence of TB transmission.

Of course, any healthcare worker with LTBI (positive TST or interferon-γ release assay, no evidence of active TB disease) should be offered treatment to reduce the risk of future TB disease (*See this month's Case Study 1*). Tuberculin skin testing should generally not be performed in individuals with a history of a strong positive result in the past. Severe reactions can be triggered with repeat skin testing in such persons.

TB in the HIV-Infected Inmate

HIV co-infection continues to be a significant challenge in treatment of persons with TB. A recent study of 367 patients with HIV/TB co-infection treated in six cities across the U.S. highlighted the difficulties encountered in treating patients with both infections.[7] Patients had been diagnosed with TB between 1986 and 2000, with 17% diagnosed in 1997 or later - a period during which potent antiretroviral therapies became available. Intolerance of TB drugs was common; 16% of patients required a change in TB treatment regimen due to drug intolerance (see this month's Case Study 2). Drug interactions were another common problem; 73% were concurrently prescribed rifamycins (rifampin, rifabutin) and HIV medications known to interact with rifamycins. Treatment was also complicated by poor adherence and concurrent liver disease. Poor adherence to TB therapy was noted in 38% of cases, and liver disease was present either prior to or during TB treatment in 25% of patients with HIV/TB co-infection. Only 62% of patients completed TB treatment and 17% of patients with HIV/TB co-infection died within 12 months of TB diagnosis.

Fortunately, understanding of pharmacokinetic interactions among drugs used to treat TB and HIV continues to improve. (Updated guidelines for concurrent HIV/TB treatment are available at www.hivatis.org. This month's IDCR-o-GRAM lists major interactions between TB and HIV therapies.) In general, the nucleoside reverse transcriptase inhibitors (NRTIs) only have minor interactions with TB drugs, and no dosing adjustments of either TB or HIV medications are necessary when using HIV regimens containing only nucleoside agents. Serum concentrations of all the available non-nucleoside (NNRTI) agents (delaviridine, efavirenz and nevirapine) are reduced by concurrent rifampin administration, and among these agents, only efavirenz is currently recommended for use in patients receiving rifampin.

A major concern has been the dosing of rifabutin with efavirenz, as both induce cytochrome P450 enzymes. A recent study provided empiric support for the recommendation to increase rifabutin dosing for TB treatment in combination with efavirenz-based regimens. The Tuberculosis Trials Consortium studied 15 patients who received standard doses of isoniazid plus rifabutin dosed 600 mg twice-weekly during the continuation phase (the last four months) of TB treatment.[8] These patients also received standard-dose efavirenz (600 mg daily) plus two NRTIs for HIV treatment.

Continued on page 4

Letter from the Editor

February 2006

Dear Corrections Colleagues,

A number of infectious diseases are concentrated among those incarcerated in jails and prisons. Of these, tuberculosis (TB) stands out, as it is a highly infectious airborne pathogen that every once in a while is resistant to one or more standard anti-mycobacterials. Procedures to prevent the spread of TB, such as the screening of inmates and staff, fitting of protective masks and maintenance of negative pressure rooms, occupy a significant amount time for many of us - as does the management of those with latent and active TB infection.

In this issue of IDCR, Duke University infectious diseases specialist Dr. Beth Gadkowski, along with Dr. Jason Stout of the North Carolina Tuberculosis Control Program review major developments in the management of TB, highlighting those areas of particular relevance to health care providers in correctional settings. After reading this issue, individuals should be able to describe techniques for TB screening and the management of TB in the HIV-infected inmate. A table of drug interactions between antiretrovirals and TB medications with recommended dose modifications accompanies the article and is worth keeping handy.

This is the final issue that Courtney Colton will serve as Managing Editor before moving on to become Development Director at a charitable organization. Since October 2004 Courtney has been responsible for getting IDCR to you and this she has done superbly. All of us at IDCR thank Courtney and wish her all the best.

As always, please feel free to send comments and suggestions to me at wohl@med.unc.edu.

Thanks,

David Alain Wohl, 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.

TUBERCULOSIS IN CORRECTIONS
(continued from page 2)

The increased rifabutin dose was adequate to compensate for efavirenz-induced increases in drug metabolism; the therapy was generally well tolerated and had potent antiretroviral activity.

Concurrent use of protease inhibitors with rifampin is no longer recommended. Although pharmacokinetic data suggested that saquinavir/ritonavir would be effective in combination with rifampin. In a recent report, the combination of saquinavir/ritonavir and rifampin was associated with 11 cases of significant transaminase elevation among 28 healthy volunteers receiving this combination, including one case that required hospitalization.[9] The saquinavir/ritonavir combination is, therefore, no longer recommended for use with rifampin. Rifabutin is the preferred rifamycin for patients taking protease inhibitors, and the dosages of rifabutin, the protease inhibitor, or both must be adjusted to compensate for the two-way interaction. (*See this month's IDCR-o-GRAM.*)

Treatment of patients with HIV/TB co-infection with potent antiretroviral therapies has led to increasing recognition of another complication: immune reconstitution inflammatory syndrome (IRIS). IRIS, defined as clinical deterioration associated with restoration of pathogen-specific immune responses, has been associated with a variety of pathogens including cytomegalovirus, hepatitis B and C, *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*), *Cryptococcus neoformans* and many others. IRIS occurs in 19% to 36% of patients with HIV/TB co-infection who receive both antituberculous and antiretroviral therapy.[10,11] A recent review of IRIS associated with mycobacterial infections identified 86 published cases of HIV/TB-associated IRIS.[12] IRIS occurred in patients with low nadir CD4 counts (median 51 cells/mm^3) and was associated with treatment-related significant increases in CD4 counts and decreases in plasma HIV RNA. However, HIV/TB-associated IRIS has been reported in patients with baseline CD4 counts as high as 435.

Extrapulmonary TB and starting antiretroviral therapy prior to completion of two months of TB treatment have also been associated with increased risk for IRIS. In contrast to IRIS associated with pathogens such as *M. avium*, most persons with HIV/TB-associated IRIS were receiving antituberculous therapy at the time of IRIS onset. Patients typically presented with fever, lymphadenopathy and worsening respiratory symptoms between two to 10 weeks after starting antiretroviral therapy. Lymphadenopathy, which could be peripheral (cervical, supraclavicular, inguinal, axillary) or intrathoracic, was present in 71% of cases. Worsening pulmonary disease, sometimes leading to respiratory failure, occurred in 28% of cases. Antiretroviral therapy was interrupted because of IRIS in 15% of cases, and 7% required surgery to treat IRIS-induced symptoms. Although some manifestations were life-threatening, no deaths due to IRIS were reported. Optimal treatment of IRIS is unclear, but 26% of patients received corticosteroids in an attempt to diminish the exuberant immune response. Recognition of IRIS and perhaps delaying antiretroviral therapy in patients with HIV/TB co-infection who do not have an urgent indication for antiretroviral treatment may reduce morbidity from this condition.

Fluoroquinolones for TB Treatment

Current guidelines recommend the use of isoniazid, rifampin, ethambutol and pyrazinamide as first-line drugs for TB treatment.[13] While the rate of multi-drug resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampin, is low in the U.S., many patients have difficulty tolerating one or more of the first-line antituberculous agents.[14] However, many of the available second-line agents are poorly tolerated and less effective than the first-line drugs. The fluoroquinolones, therefore, are increasingly promising agents for TB treatment. In fact, one of the most important predictors of successful treatment of MDR-TB is whether the TB isolate demonstrates *in vitro* susceptibility to a fluoroquinolone.[15]

A recent systematic review examined 10 randomized trials that either substituted or added fluoroquinolones to the treatment regimen for pulmonary TB.[16] Older quinolones, like ciprofloxacin and ofloxacin, were associated with a higher incidence of relapse and a longer time to sputum culture conversion when substituted for one or more first-line drugs (ofloxacin instead of rifampin in one study, ciprofloxacin instead of pyrazinamide plus ethambutol in another) in patients with TB disease sensitive to all of the first-line drugs. No difference in any significant outcome was found comparing a standard four drug regimen to four drugs plus a newer fluoroquinolone, levofloxacin, for the first two months of treatment in a patient population suspected to have high rates of drug-resistant TB. Other trials in drug-resistant TB compared fluoroquinolones (levofloxacin vs. ofloxacin and sparfloxacin vs. ofloxacin) that were either substituted or added to drug regimens. In these studies, the fluoroquinolone used did not make a significant difference with regard to cure rate or treatment failure. Importantly, regimens including fluoroquinolones were not associated with an increase in adverse events over standard regimens.

In contrast, more impressive results were reported from a recent study that substituted moxifloxacin for ethambutol during the first eight weeks of pulmonary TB treatment in sputum smear-positive patients.[17] A preliminary analysis of 301 patients enrolled in

Continued on page 6

February 2006 Case Series

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Case Study 1. Treatment of latent TB infection.

A 32 year-old nurse at your correctional facility presents for yearly TB screening. He has no symptoms, no reported contact with any inmates with TB, but his TST measures 11 mm. A review of the record reveals that his TST last year measured 0mm. Chest radiograph reveals no significant abnormalities. What should be done for this nurse?

Discussion:

The initial step after diagnosis of latent TB is *education*. The nurse should be informed that persons with a normal immune system have approximately a 5% risk to develop active TB within the first two years after infection (conversion of a negative TB skin test to positive), and another 5% risk during the rest of their lives.[19] All individuals with a positive skin test should be assessed for medical conditions that would increase the risk of progression to active TB. HIV is the single most important risk factor for progression to active disease; while ~10% of HIV-negative, otherwise immunocompetent persons will progress from TB infection to TB disease in a lifetime, ~10% of persons with HIV infection will progress YEARLY without treatment![20] All persons with latent

Continued on page 5

February 2006 Case Series
(continued from page 4)

TB infection should be offered HIV counseling and testing.

Treatment for latent TB infection usually consists of nine months of isoniazid. Isoniazid may be self-administered daily (5 mg/kg, maximum 300 mg), or may be administered directly observed twice-weekly (15 mg/kg, maximum 900 mg). Isoniazid can be hepatotoxic, causing clinically significant hepatitis in 0.1-1% of patients who take it for latent TB infection.[21, 22] Persons should be screened for symptoms of hepatitis every month while taking isoniazid, and only a 1-month supply of the drug should be dispensed at a time. Persons at risk for hepatotoxicity (e.g. HIV, viral hepatitis, alcohol use) should have transaminases drawn prior to starting isoniazid and monthly thereafter until completion of therapy (*see Case Study 2*).

Those who are allergic or intolerant of isoniazid may be offered rifampin 10 mg/kg daily (maximum 600 mg) for four months. This regimen is much more expensive than isoniazid, and rifampin interacts with many other medications, particularly antiretrovirals. A two-month regimen of rifampin plus pyrazinamide was formerly recommended, but cases of severe hepatotoxicity and death were associated with this regimen.[23] This regimen is considerably more toxic than nine months of isoniazid and is now generally not recommended for use.[24] Adherence to the nine-month regimen is generally not very good. A large study of a shorter, once weekly combination of isoniazid and rifapentine is ongoing, and hopefully will provide an alternative to the current nine-month regimen.

In this case, the nurse was tested for HIV infection and was seronegative. He started on daily isoniazid which he took for nine months with only mild elevation in ALT and AST.

Case Study 2. Intolerance of TB medications.

A 25 year-old, HIV-negative woman was placed on 4-drug therapy (isoniazid, rifampin, pyrazinamide, and ethambutol) for culture-confirmed, extensive pulmonary tuberculosis. Three weeks after initiation of therapy, she presented to sick call complaining of a diffuse rash, fever, and fatigue. Laboratory studies were significant for aspartate aminotransferase (AST) of 423 (normal 0-40), alanine aminotransferase (ALT) 652 (normal 0-40), alkaline phosphatase 135 (normal 0-150), and total bilirubin 2.2 (normal 0-1.3). She was on no other medications and denied use of over-the-counter medications available at the facility canteen, herbal remedies, alcohol, or illicit drugs. How should she be managed at this point?

Discussion

Intolerance of drugs used to treat TB is a common problem. In addition to frequent gastrointestinal symptoms, three of the four first-line TB drugs (isoniazid, rifampin, and pyrazinamide) are potentially hepatotoxic. Hepatotoxicity associated with TB drugs is idiosyncratic, often not associated with drug dosage, and may have severe consequences as illustrated in this case.

The general principles of dealing with hepatotoxicity from TB medications are listed below:

- Mild increases in transaminases are common and often of no clinical significance. TB therapy should be stopped in the following cases:
  - *ALT>3x the upper limit of normal and patient has symptoms of hepatitis OR*
  - *ALT>5x the upper limit of normal and patient is asymptomatic*

- Elevated bilirubin in the setting of elevated transaminases is a marker of more severe hepatotoxicity and should prompt immediate discontinuation of TB drugs and close monitoring.

- If TB disease is mild, therapy may be held until ALT<2x the upper limit of normal. For patients with extensive or severe TB, switch to treatment with a non-hepatotoxic regimen (e.g. streptomycin + ethambutol + moxifloxacin) while ALT improves

- Once symptoms resolve and ALT<2x the upper limit of normal, sequentially reintroduce TB drugs with close clinical and laboratory monitoring. One protocol adds back drugs 1 week apart, in the order ethambutol, rifampin, isoniazid, and pyrazinamide (order of lesser to greater potential for hepatotoxicity). In the case of severe hepatotoxicity, pyrazinamide may be omitted and the regimen extended to at least 9 months if isoniazid and rifampin are tolerated.

- Consult a TB expert if the patient cannot be treated with standard first-line therapy. Clinicians should not "make up" treatment regimens for drug intolerant patients.

- It is impossible to reliably predict which drug caused the hepatotoxicity; using a standard reintroduction protocol is essential.

- Monitoring for side effects of TB drugs should be performed no less often than monthly for patients being treated for either latent or active TB. Laboratory testing to screen for hepatotoxicity should be performed monthly only in patients at risk of hepatotoxicity (concurrent hepatotoxic drugs, chronic hepatitis, alcohol use, pregnancy, HIV).

- For patients with baseline elevated transaminases or cirrhosis, careful monitoring and expert consultation are essential. In the case of LTBI, the risks and benefits of LTBI treatment should be carefully considered prior to initiating treatment. Patients with TB disease may require alteration of the treatment regimen in concert with a TB expert.

In the above case, isoniazid, rifampin, and pyrazinamide were discontinued, and she was treated with daily ethambutol, moxifloxacin, and intramuscular streptomycin. Once the rash resolved and transaminases improved, drugs were sequentially reintroduced a week apart. The rash returned with addition of isoniazid, and the patient was successfully treated with six months of daily rifampin, pyrazinamide, and ethambutol.

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Tuberculosis in Corrections
(continued from page 4)

this study prior to January 2005 demonstrated that patients receiving moxifloxacin converted their sputum cultures to negative earlier than patients receiving ethambutol (median 43 days for moxifloxacin vs. 56 days for ethambutol, p=0.01). Moxifloxacin was generally well-tolerated: fever, nausea and dizziness were commonly reported, but seldom resulted in treatment discontinuation. These results suggest that moxifloxacin is a useful second-line agent for TB treatment, and studies are underway to examine its utility as a first-line agent.

Alternative TB Test

The Mantoux TST in which 0.1 ml of tuberculin purified protein derivative is injected into the inner surface of the forearm, is the accepted method of evaluating for TB or LTBI. However, this test may be falsely reactive in individuals who have received the Bacille Calmette-Guèrin (BCG) vaccine. The usefulness of TST is also limited by the inherent variability in its administration and interpretation. QuantiFERON-TB Gold® (QFT-G) was approved by the Food and Drug Administration (FDA) in December 2004 as a diagnostic test for active TB and LTBI. The test measures the release of interferon-gamma (IFN-gamma) when whole blood is incubated with peptides found in *M. tuberculosis*. These peptides, early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10), are secreted from *M. tuberculosis* and pathogenic *M. bovis* strains, but are not found in BCG or nontuberculous mycobacteria except *M. kansasii, M. szulgai* and *M. marinum*. As a result, QFT-G results are not affected by previous BCG vaccination or environmental exposure to nontuberculous mycobacteria. This test takes the place of the first-generation QuantiFERON® test, which is no longer being marketed.

The QFT-G test has the same logistical issues as the first generation test. Blood drawn for the test needs to be incubated less than 12 hours after being collected and lab personnel require special training to perform the assay. However, QFT-G results are available in less than 24 hours and unlike the TST, only one clinic visit is required. This makes QFT-G an attractive testing option in clinical settings such as homeless shelters and jails where follow-up can be challenging. QFT-G is also potentially a cost-effective alternative to TST testing in institutions like correctional facilities and health care settings where false positive tests can prompt additional costly testing.

The CDC released guidelines for use of QFT-G in December 2005 (see Resources).[18] According to these guidelines, QFT-G may be used in all circumstances in which the TST is currently used, including contact investigations, targeted TST of high-risk groups such as immigrants, surveillance screening (such as in healthcare workers or correctional facilities), or as an aid to diagnosis of TB disease. However, there is a paucity of data to support the use of the test among immunocompromised persons (e.g. HIV-infected, those on chronic corticosteroids, recipients of tumor necrosis factor-alpha inhibitors, etc.) or in children. Furthermore, while the QFT-G is likely more specific than the TST for LTBI, it may be less sensitive than the TST for detection of LTBI. Use of QFT-G instead of the TST in the correctional setting, particularly in the setting of a significant foreign-born incarcerated population, seems attractive, but careful attention should be paid to quality assurance and impact on correctional system healthcare costs.

Conclusions

Despite continued decline in TB in the U.S. as a whole, TB will continue to be a significant problem within the correctional system. Available data indicate that greater attention to the development and implementation of systems is urgently needed to ensure prisoners and former inmates complete TB treatment. Further, continued vigilance and adherence to good infection control policies in prisons and jails will be vital to protecting correctional healthcare workers as well as others in the correctional setting. New diagnostic tools, including blood tests for TB infection, are becoming available to improve TB diagnosis, but much work remains to be done. Shorter and better tolerated regimens are needed for treatment of both latent and active TB. Treatment of persons co-infected with HIV/TB continues to be challenging because of high pill burden, drug interactions and tolerability, but as HIV treatment is simplified, some of these challenges may be overcome. IRIS is another important challenge for HIV/TB co-infected patients, and trials of different treatment strategies to optimize IRIS management, including the sequencing of TB and HIV therapy, are underway. The key to TB control is to improve diagnosis and treatment in countries where TB is highly endemic; only by controlling TB in the rest of the world is there any hope of eliminating TB in the US.

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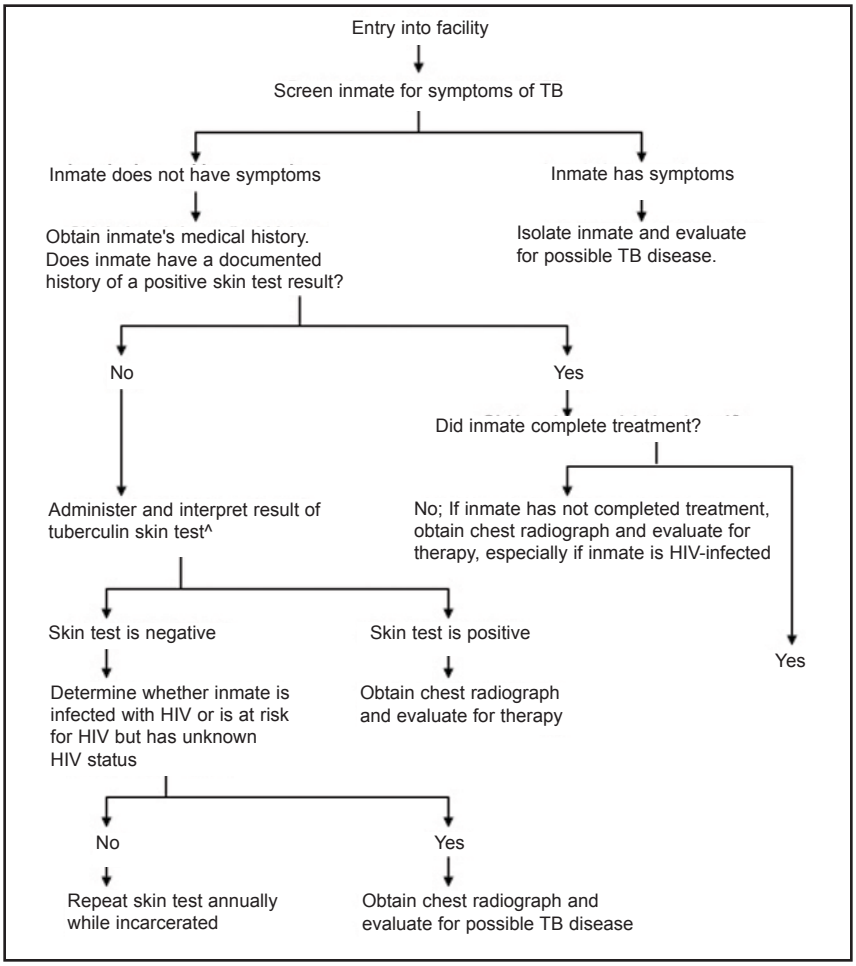
IDCR-o-GRAM

Protocol for Screening Inmates for TB in Long-Term Correctional Facilities



^In some correctional facilities two-step testing for initial testing may provide a more reliable baseline.

Note: Treatment of latent TB infection is only indicated when the PPD is positive. The criteria for a positive PPD are different depending on HIV status but suspicion of contact (e.g. with active, contagious TB case) or PPD > 5 mm are the criteria for latent TB infection treatment of HIV seropositives and PPD > 10 mm is criteria for such treatment of non-immunocompromised inmates.

Adapted from: CDC. Prevention and control of tuberculosis in correctional facilities recommendations of the advisory council for the elimination of tuberculosis. MMWR. 1996; 45(RR-8):1-27.

TB101: Rifamycin Dosing in TB/HIV Co-infection

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

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Disclosures: **Consultant: Pfizer, Speaker's Bureau: Gilead Sciences, Abbott Laboratories; **Speaker's Bureau: Gilead, Boehringer-Ingelheim*

	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%

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

* 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.

References:
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Last accessed January 23, 2006 from http://aidsinfo.nih.gov/guidelines/adult/AA_100605.pdf
TB/HIV Drug Interactions. Last accessed January 23, 2006 from http://www.cdc.gov/nchstp/tb/TB_HIV_Drugs/Table1.htm
TB/HIV Drug Interactions. Last accessed January 23, 2006 from http://www.cdc.gov/nchstp/tb/TB_HIV_Drugs/Table2.htm
TB/HIV Drug Interactions. Last accessed January 23, 2006 from http://www.hiv-druginteractions.org/frames.asp?drug/drg_main.asp

Save the Dates

Politics on Paper - Global Tragedies/Personal Perils. Featuring the work of Eric Avery MD, John Risseeuw and Robbin Ami Silverberg.
January 13 - March 11, 2006
Columbia College Chicago
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1104 S. Wabash Ave
Chicago, IL 60605
Phone: 312.344.6684

13th Annual Conference on Retroviruses and Opportunistic Infections
February 5-9, 2006
Denver, Colorado
Visit:www.retroconference.org

13th Annual Ryan White National Youth Conference on HIV/AIDS
February 18-20, 2006
Philadelphia, Pennsylvania
Visit: www.napwa.org/rwnyc/

National Conference on African-Americans and AIDS
February 27-28, 2006
Philadelphia, PA
Visit: www.minority-health-care.com/

NIMH/IAPAC Conference on HIV Treatment Adherence
March 8-10, 2006
Jersey City, New Jersey
Visit: www.hivadherenceconference.com

World TB Day
March 24, 2006
Visit: www.stoptb.org

Updates in Correctional Health Care
April 8-11, 2006
Las Vegas, Nevada
Visit: www.ncchc.org

Satellite Videoconference "Hepatitis B & C with HIV Co-infection"
April 19, 2006
12:30-2:30 EST
CME-accredited webstream of last conference available on-line
Visit: www.amc.edu/patirnt/hiv/hivconf/index.htm

ACHSA 2006 Multidisciplinary Training Conference
May 11-13, 2006
Durham, North Carolina
Visit: www.achsa.org

News and Literature Reviews

TB Rates Higher in Prison Systems than General Population

A recent study analyzed data reported to the national tuberculosis (TB) surveillance system from 1993 through 2003 and sought to describe disparities and trends in TB risk factors and treatment outcomes between correctional inmate and non-inmate populations. Of the 210,978 total reported United States TB cases, 3.8% were from correctional systems. Federal and state prison case rates were 29.4 and 24.2 cases per 100,000 inmates, respectively, which was considerably higher than those in the non-inmate population (6.7 cases per 100,000 persons.) Inmates with TB were more likely to have at least one TB risk factor (excess alcohol use, injection drug use, non-injection drug use, homelessness and HIV) compared with non-inmates (60.1% vs. 42.0%) and to receive directly observed therapy (DOT) (65.0% vs. 41.0%). However, inmates were less likely to complete treatment within 12 months compared with non-inmates (76.8% vs. 89.4% in 2001). Rates of completion of therapy within 12 months were lower in persons with TB risk factors and lowest for those who had HIV infection at the time of TB diagnosis, in both inmates and non-inmates, but lower among inmates. The authors concluded that TB case rates in prison systems remain higher than in the general population and that inmates with TB are less likely than non-inmates to complete treatment.

MacNeil JR, Lobato MN, Moore M. An unanswered health disparity: tuberculosis among correctional inmates, 1993 through 2003. Am J Pub Health. 2005; 95(10):1800-5.

San Francisco Jail Inmates 59x More Likely to Develop Active TB

In a recent study, White, et al, measured rates of development of active TB and completion of TB therapy over five years in a cohort of inmates. The participants completed a randomized trial in 1998-1999 comparing education/incentive versus usual care to improve therapy completion after release from the San Francisco County Jail (SFCJ). Records from the SFCJ, the County TB Clinic and the California TB Registry were used to measure therapy completion and development of active TB. Of a total of 557 inmates, 31.6% completed therapy, of whom 59.7% did so in jail, during the term of the randomized trial or in subsequent incarcerations. Subjects who reported their country of birth as Mexico were least likely to finish therapy as compared to those from Central or South America, South-east Asia or the United States. Previous therapy for TB and greater education were both associated with TB therapy completion. Three subjects developed active TB during the five years of follow-up, resulting in an annual rate of 108 per 100,000 inmates. The standardized mortality ratio calculated against the California case rate for 2003 (9.1 per 100,000) indicates that this sample was 59 times as likely as those in the general California population to develop active TB. Study authors concluded that the high rate of TB seen in this jail cohort emphasizes the importance of screening for active TB, as well as improving efforts to ensure treatment completion.

White M, Tulsky J, Menendez E, et al. Incidence of TB in inmates with latent TB infection: 5-year follow-up. Am J Prev Med. 2005; 29(4):295-301.

Avoid Use of Rifampin with Atazanavir/Ritonavir

According to recent reports, the combination of Rifampin with Atazanavir (ATV) is no longer recommended. Atazanavir is metabolized largely via cytochrome P450 (CYP) 3A4 while Rifampin is known to be a strong inducer of CYP3A4. Therefore, unboosted ATV should not be prescribed with rifampin. Mallolas, et al hypothesizing that boosting ATV with low-dose ritonavir (a CYP3A4 inhibitor) would negate the effect of rifampin on ATV levels studied HIV-infected adults with a viral load <200 copies/mL while receiving a triple nucleoside regimen as well as 300 mg of rifampin daily as part of a TB regimen. ATV at a dose of (300 mg)/ritonavir (100 mg) per day was added and a complete pharmacokinetic study of ATV was performed three weeks later. In all of the first three of a total of eight planned patients who enrolled in the study, the plasma ATV Cmin, Cmax and AUC were undetectable. Study authors concluded that even in the presence of a low dose of ritonavir, there are clinically significant interactions between ATV and rifampin leading to a near absence of detectable ATV in the plasma. Rifampin should not be administered together with ATV even when the latter is ritonavir-boosted.

Mallolas J, Nomdedeu M, Soriano A, et al. Pharmacokinetic interaction between rifampin and the combination of atazanavir and low dose ritonavir in HIV-infected patients. Poster 123. 45th Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, DC. December 17, 2005.

Resources

CDC Prevention and control of tuberculosis in correctional facilities recommendations of the advisory council for the elimination of tuberculosis.
MMWR. 1996; 45(RR-8):1-27.

Centers for Disease Control Division of Tuberculosis Elimination.
http://www.cdc.gov/nchstp/tb/

CDC Guidelines for using the QuantiFERON®-TB gold test for detecting mycobacterium tuberculosis infection, United States.
MMWR. 2005; 54(RR15):49-55.

CDC Guidelines for the investigation of contacts of persons with infectious tuberculosis: national tuberculosis controllers association and CDC.
MMWR. 2005; 54(RR15):1-37.

TB Education and Training Resources Center
http://www.findtbresources.org/scripts/index.cfm

CDC Appendix B: Recommendations for the investigation of contacts of persons with infectious tuberculosis (TB.)
MMWR. 2005; 54(RR15):43-47.

CDC Targeted tuberculin testing and treatment of latent tuberculosis infection.
MMWR. 2000; 49(RR6):1-54.

CDC Treatment of tuberculosis.
MMWR. 2003; 52(RR11):1-77.

The Body Tuberculosis Fact Sheet Number 518.
Available at: http://www.thebody.com/nmai/pdfs/tb.pdf

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 February 28, 2006. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. According to national data the prevalence of TB disease (i.e. active TB) among inmates is:
   - A. Half the rate of the non-incarcerated
   - B. The same as the rate of the non-incarcerated
   - C. 2 times the rate of the non-incarcerated
   - D. Over 3 times the rate of the non-incarcerated

2. Each of the following statements regarding drug-drug interactions between antiretrovirals and TB medications are true EXCEPT:
   - A. Nucleoside reverse transcriptase inhibitors (NRTIs) have only minor interactions with TB medications
   - B. Serum concentrations of all non-nucleoside reverse transcriptase inhibitors (NNRTIs) are reduced by rifampin
   - C. When administered with efavirenz the dose of rifabutin must be lowered
   - D. Rifampin should generally not be co-administered with protease inhibitors
   - E. None of the above

3. The following statements regarding the two-step tuberculin skin testing are TRUE:
   - A. This procedure helps identify prior remote TB infection
   - B. Should be considered for correctional healthcare workers at the time of hire
   - C. Is well suited for use among inmates of jails and those frequenting homeless shelters
   - D. A and B
   - E. A and C

4. Patients who develop an increase in ALT during treatment of TB disease should:
   - A. Stop TB therapy if the ALT>3x the upper limit of normal and patient has symptoms of hepatitis
   - B. Stop TB therapy if the ALT>5x the upper limit of normal and patient is asymptomatic
   - C. Restart TB therapy, if therapy is stopped, once symptoms resolve and ALT<2x the upper limit of normal with sequential reintroduction of TB drugs and close clinical and laboratory monitoring.
   - D. All of the above

5. All inmates with diagnosed with HIV infection should be prescribed treatment for latent TB regardless of tuberculin skin testing result (TRUE or False)?
   - A. True
   - B. False

IDCR Evaluation

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

3. What future topics should IDCR address?

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