Welcome to the “TB Clinic” for the opportunity to learn about TB Control!

LOGISTICS

Location: TB Clinic (the waiting room), Harborview Medical Center, Ground floor, East Clinic Wing (9th Avenue & Alder Street entrance across from HMC R&T Building). We are across the hall from the Endocrine/Cardiology Clinic and next door to the Gamma Knife suite.

Time: The case review on Wednesdays starts at 8:30 am and will end by 10:00 am. However, the case review is usually cancelled on the third Wednesday of each month because of our monthly staff meeting. Please come at least 5 minutes before the meeting starts. The door to the clinic is locked; should you be late, please pick up the phone on a wall and wait for an attendant to escort you into the clinic area.

Communication: On Monday or Tuesday prior to attending, please send an email to both of the following addresses to confirm that case review will, in fact, occur.

masa.narita@kingcounty.gov  (Masa Narita, MD; Tuberculosis Control Officer and Program Director, Public Health -Seattle & King County [PH-SKC]; Associate Professor, Division of Pulmonary & Critical Care Medicine, UW School of Medicine)

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BACKGROUND

The TB Clinic is operated by the TB Control Program, PH-SKC. The mission of TB Control Program is to interrupt TB transmission in King County. The highest priority of our program is to identify persons with highly suspected or confirmed infectious TB and to ensure adherence to and completion of their TB treatment. The second highest priority is to evaluate close contacts of infectious TB cases, and ensure treatment for TB infection if indicated. Our third priority is to complete the local TB medical evaluation of immigrants and refugees whose overseas chest X-rays for visa requirement showed abnormalities consistent with “inactive” pulmonary TB.
FUNDING

TB Control is part of government activities. Our activities are supported by Seattle & King County (tax revenues for basic infrastructure and operations mandated in the WA state law), the Washington State Department of Health (laboratory services and surveillance support), and the Centers for Disease Control and Prevention (grants for surveillance, control, and research). As a mandatory, government-funded disease control operation, treatment of infectious TB patients is a priority of our duty and mission to protect public health, which carries personal health benefits for the patient as well. This legal and financial basis for program activity also drives the objectives, means, scope, and limitations of our patient-care activity.

Due to ongoing financial challenges, the TB Clinic focuses its resources on TB cases with highly suspected or proven pulmonary involvement (i.e. contagious to others). We collaborate with Harborview Medical Center and community-based infectious diseases specialists and our local experts provide medical management for extrapulmonary-only cases (i.e., non-infectious TB).

CASE REVIEW CONTENT AND PURPOSE

We systematically review all confirmed TB cases as well as persons highly suspected of having active TB who reside in King County on a routine basis at 2, 8, and 14 weeks into TB treatment and thereafter every 3 months until treatment is completed. For cases with pulmonary involvement, a case management team (nurse case manager, disease intervention specialist [DIS] and outreach worker) is assigned to each patient and the nurse case manager usually presents the case. For extrapulmonary-only cases, a data specialist and the medical director track the patient’s progress on a periodic basis and the medical director presents the case during routine reviews.

The TB Control Officer (Dr. Masa Narita) convenes and directs the meeting. Other attendees include nurse case managers, disease intervention specialists (DIS), outreach workers, medical director (Dr. Chris Spitters), TB program manager, epidemiologists, clinic staff (clinic nurse, medical assistants), and guests.

The medical component of a case’s review includes basic demographic information, the basis for the TB diagnosis, HIV status, other major medical problems, TB treatment to-date, adherence, tolerance, and response to therapy. The focus of the discussion then turns to address barriers to adherence (i.e., psychosocial, behavioral, medical, and economic issues that interfere with the patient’s adherence with the management plan). The discussion then closes with a review of progress and findings from the contact investigation.
LEARNING RESOURCES

The following ATS/CDC guidelines are recommended for clinicians who provide TB care in the United States and other high-income nations:

- Diagnostic Standards and Classification of TB in Adults and Children
- Treatment of Tuberculosis
- Targeted Testing and Treatment of Latent Tuberculosis (with post-publication updates advising against routine use of rifampin/pyrazinamide regimen)
- Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection
- Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis
( All can be accessed via: http://www.cdc.gov/tb/ )

International Guidelines for Providers Serving Patients in Low-income Countries (global health oriented)
- International Standards for TB Care
- Treatment of Tuberculosis Guidelines (WHO)
- Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings (WHO)
( All can be accessed via: http://www.who.int/tb/en/ )

Web-based Learning Tools
- Core Curriculum on Tuberculosis. What the Clinician Should Know.  
  ( http://cdc.gov/tb/education/corecurr/index.htm )
- Curry International Tuberculosis Center  
  ( http://www.nationaltbcenter.edu/products/a-z_list.cfm )

Other relevant Websites
http://www.tstin3d.com (useful for decision-making on treatment for latent TB infection)

COMMON TB JARGON USED IN CASE REVIEW

- **AFB** (acid-fast bacilli). Due to the long carbon chains in the waxy cell wall of mycobacteria, these organisms can retain dyes within the bacilli that usually are removed from other microorganisms by alcohols and mineral acids (e.g., hydrochloric acid). Thus, they are “acid-fast”.

- **BCG** (Bacille Calmette-Guerin). The TB vaccine administered at birth in most low- and middle-income countries. BCG’s main benefit is in protecting small children from developing severe and fatal forms of TB. It’s efficacy in preventing pulmonary TB is controversial and estimated at 0-50%, depending on the strain used, the location of the study, and the era when the study was conducted.
- **ATS/CDC TB Classification System**
  - Class 0: not infected
  - Class 1: exposed to infectious TB (in the last 3 months) and not infected (and the completion of repeat latent TB evaluation pending)
  - Class 2: latent TB infection
  - Class 3: active TB disease (confirmed)
  - Class 4: old, inactive TB
  - Class 5: suspected TB disease

- **Class B.** Prior to immigration to the U.S., (1) immigrants who apply for permanent legal resident (aka: “green card”) visa status and (2) refugees must undergo chest X-ray overseas through a health care provider contracted by United States Department of State. The TB screening takes place commonly at a large hospital in the foreign nation’s capital that also provides TB care (e.g., St. Luke’s Hospital in Manila, Choray Hospital in Ho Chi Minh City). If the chest X-ray is abnormal, sputum specimens are collected for AFB smear (and in many countries, AFB culture as well).
  - If the applicant is diagnosed with active pulmonary TB, the applicant is designated “Class A” and entrance to the US restricted until TB treatment is either completed through that facility, or given for sufficient duration to render them non-infectious.
  - If the CXR is abnormal and consistent with pulmonary TB but the sputum specimens are negative for AFB on smear (and culture, if done), they are called “Class B” and may travel but need to complete follow-up evaluation in the U.S.

- **Culture-negative, clinical case of TB.** A patient with a clinical and radiographic findings suggestive of TB, a positive tuberculin skin test or QuantiFERON TB Gold In-Tube test, negative AFB cultures, and clinical or radiographic improvement with TB therapy. Approximately 10% of pulmonary TB cases and 30% of extrapulmonary-only TB cases are culture-negative but clinically diagnosed.

- **DOT** (directly observed therapy). In its strictest interpretation, this is the face-to-face, witnessed ingestion of tuberculosis medications by a responsible entity (usually a PHSKC employee). The goals of DOT are two-fold: (1) documenting ingestion for medical and public health purposes and (2) routinely monitoring patient tolerance and ensuring patient safety. Alternative modes of treatment observation that aim to provide a similar level of verification and safety include delegated DOT (e.g., to a pharmacist, responsible third party who is not a healthcare professional), two-way analog videophone, and secure internet video encounters. DOT is not typically applied to extrapulmonary-only cases in
King County, while several factors (fiscal, legal, public health protection etc) were taken into consideration.

- **DRSS** (Drug Resistant Screening by Sequencing): The Washington State Public Health Laboratories (WAPHL) developed in-house capacity to perform DNA sequencing-based screening for mutations associated with resistance to isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA).

- **IGRA** (Interferon Gamma Release Assay). These are whole blood assays for the detection of *M. tuberculosis* infection. The test measures ex-vivo production of interferon gamma released by patient’s lymphocytes after incubation with TB antigens, ESAT 6, CFP 10, and TB 7.7. Like the TST, they do not discriminate between latent TB infection and active TB disease. Two IGRA's are available commercially: (1) QuantiFERON TB Gold *In Tube* (also called “QFT”) and (2) T-Spot. Sensitivity in active TB is estimated at about 75-80% (similar to TST and with all the same caveats about false negatives). Specificity is much higher than that of TST because the antigens used by IGRA's are present neither in BCG nor in most non-TB mycobacteria (except for *M. marinum, M. kansasii, and M. szulgai*). IGRA's are preferred over TST for patients with a history of BCG vaccination.

- **NAAT** (nucleic acid amplification test): AMTD and Amplicor are two FDA-approved, commercially available NAAT's. The Washington State Department of Health’s Public Health Laboratories has offered its in-house NAAT since August 2011. In prior years, the Public Health Laboratory used AMTD. UWMC Laboratory Medicine also offers an in-house PCR for *M. tuberculosis*. NAAT’s specificity is high (over 90-95%) and sensitivity to detect TB is better than AFB smear (AFB smear 50%, NAAT 70-80%, culture 90-95%)

- **TST** (tuberculin skin test).

- **PPD** (purified protein derivative). This is the material injected intra-dermally for a tuberculin skin test.

- **SIRE** or **SIREZ**. This acronym corresponds to the first or dominant letter for first-line drugs routinely analyzed in TB drug susceptibility testing (DST): Streptomycin, Isoniazid, Rifampin, Ethambutol, pyrazinamide. Please note that WHO, CDC, ATS, and IDSA literature and guidelines more commonly designate isoniazid as “H” (from the chemical name, isonicotinylHydrazine). An isolate which is “SIREZ-sensitive” or “HRESZ-sensitive” is fully susceptible to first-line anti-TB drugs; also called “pan-sensitive”.


- **TBESC:** TB Epidemiologic Studies Consortium. The TB Clinic participates in CDC-sponsored multicenter research on latent TB infection. The study offers TST, QFT and TSpot to patients at high-risk of TB (e.g., close contacts of an infectious TB case), and follows the study subjects for two years. The aims are to prospectively compare the TST and IGRA in diagnosing TB infection and in predicting progression to TB.

- **Window Period Prophylaxis:** When a small child (younger than 5 years old) or a severely immunocompromised person (e.g., HIV) is identified as a close contact of an infectious TB case and their first TST/QFT is negative, they may be placed on INH (or any other preventive treatment) until repeat TST/QFT is performed 8-10 weeks after the last exposure. The reason is that it may take up to 8-10 weeks for those who have acquired TB infection to convert their TST/QFT, and a small child/immunocompromised can progress to active TB rapidly. In the majority of severely immunocompromised persons, preventive treatment may have to be completed (e.g., INH 6 -9 months, Rifampin 4 months) as even the second TST/QFT may not be reliable.