DOH 343-071 June 2012
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Washington State

TUBERCULOSIS SERVICES MANUAL

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FORMS

GLOSSARY

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• TB Consultation Form

About the *Washington State Tuberculosis Services Manual*

Purpose

The tuberculosis (TB) services manual is intended to assist Washington State health care in providing the highest level of care possible, according to national/state guidelines and recommendations. Responsibility for the quality of care for TB patients belongs to the nurse case manager and treating physician.

Audience

The most likely readers of this manual are people working in the health field. This may include, but is not limited to:

- Nurses (clinic, hospital, city, county, regional public health)
- Physicians (health officers, physician consultants, physician's assistants, ARNP)
- State TB services staff
- Indian Health Services staff
- Public Health Officers
- Epidemiologists
- Outreach workers

This manual provides guidelines, recommendations, and examples from national, state, and local groups. Where there is a need for more information available a hyperlink is provided for you. A hyperlink is a reference to another document that will take you to that location. Click on the link to read more about the topic.

In Washington State, TB control is governed by state law and rule. You may find information on TB laws in Washington State in the Revised Code of Washington (RCW) 70.28.005 and the Washington Administrative Code (WAC) 246-170.

How to Use This Manual

Portable Document Format

This manual is available electronically as a portable document format (PDF) file. To view the PDF file, you will need the free Adobe Reader, available at http://www.adobe.com/products/acrobat/readstep2.html.

Hyperlinks

When viewing this manual online with an Internet connection, you can go directly to underlined Web addresses by clicking on them.

Cross-References

When viewing this manual electronically, you can go directly to other sections or topics in the manual by clicking on text next to this icon:

Forms

Required and recommended forms are available as links in the specific chapters and in the **FORMS** section of the manual.

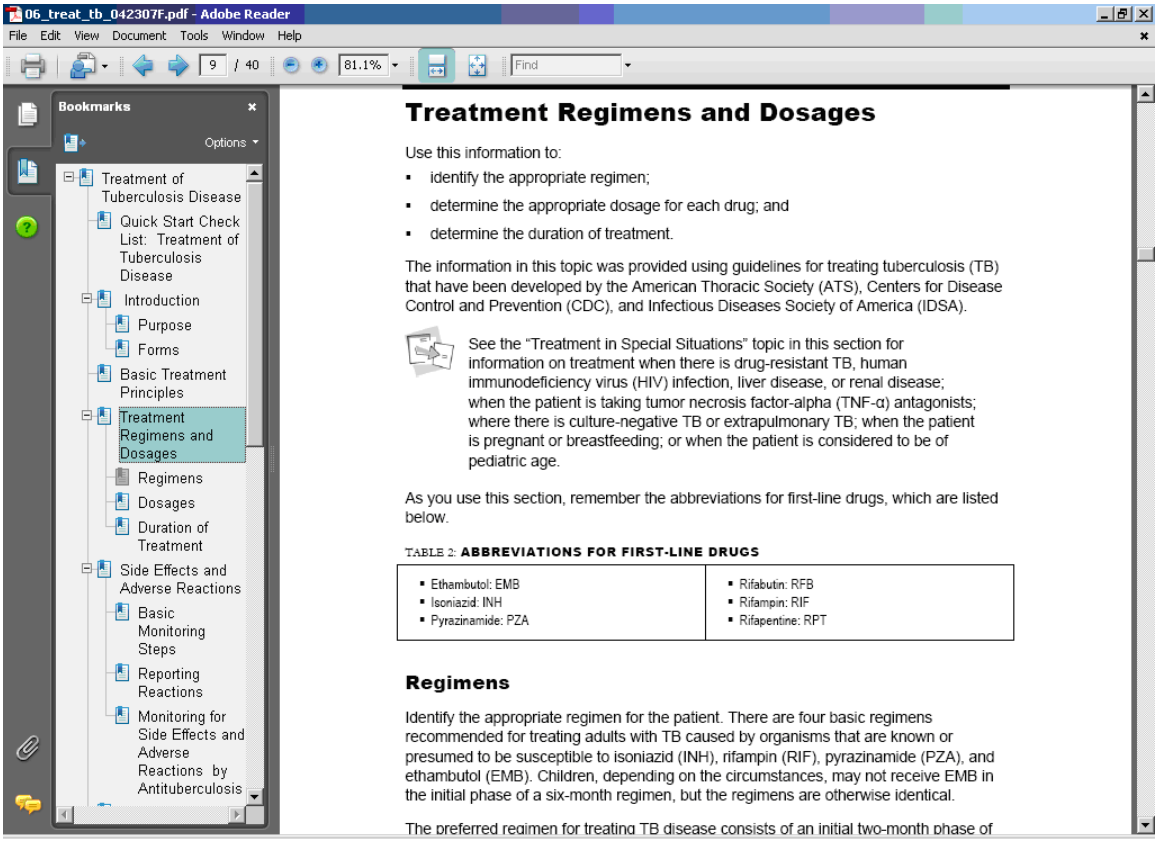
Bookmarks

In PDF files, you can use bookmarks to go quickly to a section or topic. If the bookmarks are not visible on the left, click the Bookmarks icon or tab on the left of the window.

To view sections and topics in the bookmarks list:

- Click + to see a more detailed list.
- Click – to hide the more detailed list.

To go to a section or topic in the bookmarks list, point to its name and left-click.



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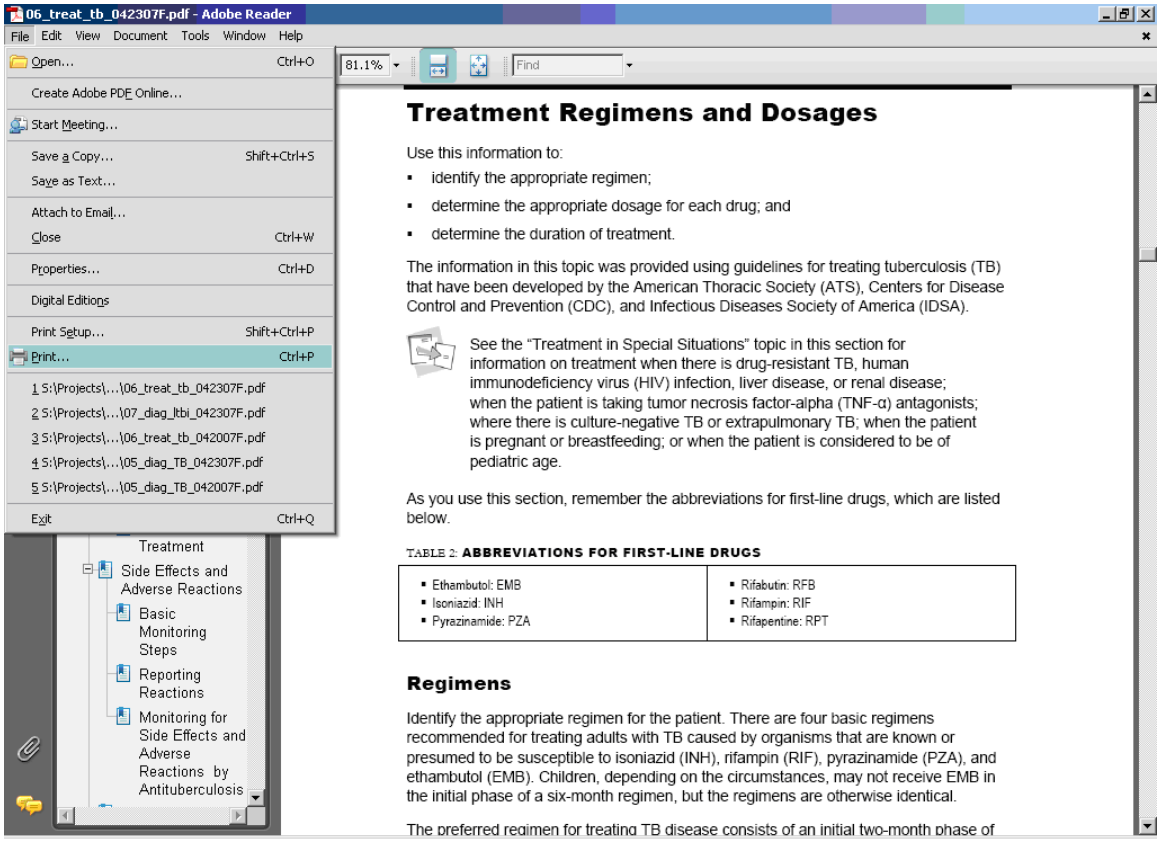

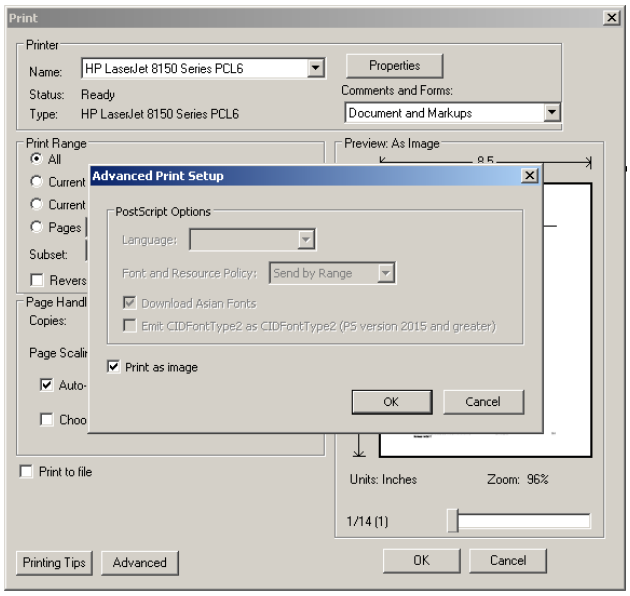

Some printers have older printer drivers that cause spaces to appear in the middle of words. To avoid this problem, select File/Print, click the advanced button, check Print as Image, and then click OK. If you need further assistance with printing, call the Curry International Tuberculosis Center's IT staff at 415-502-5810.

Icons

Throughout the manual, these icons quickly cue you about important information and other resources:

This warns about high-consequence information you must understand when performing the task.

This signals when you should call to report or to consult on the task.

This highlights special considerations for pediatric patients.

This suggests another relevant area in the manual or another resource that you may want to review.

This alerts you that a form is available for the task.

Abbreviations

Refer to the list below for abbreviations used in the manual.

ACET	Advisory Council for the Elimination of Tuberculosis
ACH	air changes per hour
AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
AII	airborne infection isolation
ALT	alanine aminotransferase
ARPE	*Aggregate Report for Program Evaluation*
ART	antiretroviral therapy
AST	aspartate aminotransferase
ATS	American Thoracic Society
BAMT	blood assay for *Mycobacterium tuberculosis*
BCG	bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention
CT	computed tomography
CXR	chest radiograph
DNA	deoxyribonucleic acid
DOT	directly observed therapy
DRSS	drug resistance screening by sequencing
DTBE	Division of Tuberculosis Elimination
DTH	delayed-type hypersensitivity
ED	emergency department
EMB	ethambutol
EMS	emergency medical service
ESRD	end-stage renal disease

FDA	U.S. Food and Drug Administration
HAART	highly active antiretroviral therapy
HCW	healthcare worker
HEPA	high-efficiency particulate air
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
IDSA	Infectious Diseases Society of America
IGRA	interferon gamma release assay
INH	isoniazid
LTBI	latent tuberculosis infection
M. tuberculosis	Mycobacterium tuberculosis
MDR-TB	multidrug-resistant tuberculosis
MIRU	mycobacterial interspersed repetitive units
MOTT	mycobacterium other than tuberculosis
NAA	nucleic acid amplification
NIOSH	National Institute for Occupational Safety and Health
NNRTI	nonnucleoside reverse transcriptase inhibitors
NTCA	National Tuberculosis Controllers Association
NTNC	National Tuberculosis Nurse Coalition
NTM	nontuberculous mycobacteria
OSHA	Occupational Safety and Health Administration
PAPR	powered air-purifying respirator
PCR	polymerase chain reaction
PHIMS	Public Health Issue Management System
PHSKC	Public Health Seattle - King County
PI	protease inhibitor
PPD	purified protein derivative

PZA	pyrazinamide
QA	quality assurance
QFT	QuantiFERON®-TB test
QFT-G	QuantiFERON®-TB Gold test
RFB	rifabutin
RFLP	restriction fragment length polymorphism
RIF	rifampin
RNA	ribonucleic acid
RPT	rifapentine
RVCT	Report of Verified Case of Tuberculosis
RZ	rifampin and pyrazinamide
SHD	Snohomish Health District
TPCHD	Tacoma – Pierce County Health Department
TB	tuberculosis
TNF-α	tumor necrosis factor-alpha
TST	tuberculin skin test
TU	tuberculin units
USCIS	U.S. Citizenship and Immigration Services
UVGI	ultraviolet germicidal irradiation
XDR-TB	extremely drug-resistant tuberculosis

Purpose of Tuberculosis Control

Tuberculosis (TB) is caused by a bacterial organism named *Mycobacterium tuberculosis* (These organisms are sometimes called tubercle bacilli). Mycobacteria can cause a variety of diseases. Some mycobacteria are called tuberculous mycobacteria because they cause TB or diseases similar to TB. The MTB complex consists of *M. tuberculosis, M. bovis, M. africanum, M. microti, M. canetti, M. pinnipedi.* Tuberculosis mycobacteria readily spread from person to person. Other mycobacteria are called nontuberculous mycobacteria (NTM) because they do not cause TB. One common type of nontuberculous mycobacteria is *M. avium* complex. Tuberculous mycobacteria readily spread from person to person; nontuberculous mycobacteria do not usually spread from person to person.

The goal of TB control in the United States is to reduce TB morbidity and mortality by doing the following:

- Preventing transmission of *M. tuberculosis* from persons with contagious forms of the disease to uninfected persons, and
- Preventing progression from latent TB infection (LTBI) to active TB disease among persons who have been infected *M. tuberculosis* infection.[1]

For information on the transmission of *M. tuberculosis* and on how LTBI progresses to TB disease, see the Centers for Disease Control and Prevention's (CDC's) *Core Curriculum on Tuberculosis* (2011) at: http://www.cdc.gov/tb/education/corecurr/index.htm

The four fundamental strategies to reduce TB morbidity and mortality include the following:

1. Early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment
2. Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen
3. Identification of other persons with latent TB infection at risk for progression to TB disease, and treatment of those persons with an effective drug regimen
4. Identification of settings in which a high risk exists for transmission of *M. tuberculosis* and application of effective infection control measures[2]

For more information on these strategies and the thinking behind them, see "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America" (*MMWR* 2005;54[No. RR-12]) at: http://www.cdc.gov/MMWR/PDF/rr/rr5412.pdf .

Washington State Laws and Rules on Tuberculosis Control

Washington State laws and rules on tuberculosis (TB) are located in the Washington Administrative Code (WAC) and the Revised Code of Washington (RCW).

In the WAC, see Chapter 246-170 (Tuberculosis Control) in Title 246 (Department of Health) at: http://apps.leg.wa.gov/WAC/default.aspx?cite=246-170

In the RCW, see chapter 70.28 (Control of Tuberculosis) at: http://apps.leg.wa.gov/RCW/default.aspx?cite=70.28

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at: http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Contact Washington State TB Services at 360-236-3443 for assistance with interpreting Washington State laws and rules regarding TB control.

National/State Indicators & Measures

Core Objectives	Target	Origin of Indicator	Definition
Index of Completion at 12 months- For whom 12 months or less TX indicated	WA-93% NTIP- 93%	NTIP	Percent of patients with newly diagnosed TB for whom 12 months or less of treatment is indicated who complete treatment.
Sputum Culture Conversion	NTIP- 61.5%	NTIP	Percent of TB patients with positive sputum culture results who have documented conversion to sputum culture-negative within 60 days of treatment initiation
Sputum smear (+) Result to Starting TB Medications	7 days 100%	NTIP	Percent of TB patients with positive AFB smear results from a respiratory specimen who initiate treatment within 7 days of specimen collection. Reported for all smear (+) cases—including respiratory specimens such as sputum, BAL and bronchial washing.
Total Contacts Evaluated	WA- 93% NTIP- 93%	NTIP	Percent of contacts to sputum AFB smear-positive TB patients who are evaluated for infection and disease Completed evaluation could refer to any of the following: 1) contacts that were TST/QFT tested <8 weeks after exposure once and if not infected on first test, tested again ≥ 8 weeks after exposure. If they were infected on their first test, they were followed-up with a chest x-ray. If they tested positive on their second TST/QFT test, that test was also followed up with a chest x-ray. 2) contacts that were TST/QFT tested once at least 8 weeks after the exposure. If they were newly infected on the test, they were followed-up with a chest x-ray. 3) Prior positive contacts with documented positive TST/QFT results have a symptom screen and if symptomatic have a chest x-ray.
Contacts Who Started LTBI Treatment who Complete Treatment	NTIP- 79%	NTIP	Percent of contacts to sputum AFB smear-positive TB patients who have started treatment for the newly diagnosed LTBI, increase the proportion who complete treatment. (completion of a recommended regimen of INH, Rifampin, or Rifapentine/INH, or a recommended regimen for drug-resistant TB)
Treatment Failure Rates and Relapse Rates	WA-≤ 10%	WA	Among all cases undergoing or having completed treatment those who fail treatment (defined as continued or recurrently positive cultures during the course of antituberculosis therapy, whose sputum cultures remain positive after 4 months of treatment) or relapse (defined as the circumstance in which a patient becomes and remains culture negative while receiving therapy but, within 12 months after

			completion of therapy, either becomes culture positive again or has clinical or radiographic deterioration that is consistent with active tuberculosis).
Measures	**Measurement**	**Origin of Indicator**	**Definition**
Reporting of HIV status	Percent	NTIP	Among all cases; the percent for whom a definitive (i.e. positive or negative) HIV status is reported.
Drug Sensitivity Results Reported	Percent	NTIP	Percent of culture-positive TB cases with initial drug susceptibility results reported
Sputum Culture Reported	Percent	NTIP	Percent of TB cases with a pleural or respiratory site of disease in patients ages 12 years or older that have a sputum-culture result reported
Culture Specimen Collection to Arrival at Lab	Mean, Median, Mode	WA	Among cases from whom any culture specimen is collected—the time from which the first viable culture specimen was collected to the time the specimen was received at the initial processing lab.
Report of (+) Sputum Smear Results to LHJ	Mean, Median, Mode	WA	Among sputum smear (+) cohort cases—the time from which the smear positive specimen was collected to the date the LHJ is notified of sputum smear (+) results.
Report of (+) Culture Results to LHJ	Mean, Median, Mode	WA	Among culture (+)cases—the time from which the culture positive specimen was collected to the date the first culture (+) result is reported to the LHJ.
Report of DST to LHJ on positive culture	Mean, Median, Mode	WA	Among culture (+) cases—the time from culture (+) specimen collection to the date in which 1st-line DST results are reported to LHJ.
Sputum smear + Receiving Appropriate DOT	Percent	WA/King	Among cases initiating treatment who are sputum smear positive—the percent who have received 90% or more of non-holiday weekday doses under directly-observed therapy (DOT) during their treatment course.
Recommended Initial Therapy	Percent	NTIP	Percent of patients who are started on the recommended initial 4-drug regimen when suspected of having TB disease
Universal Genotyping	Percent	NTIP	Percent of culture-confirmed TB cases with a genotyping result reported
Genotyping TAT	Mean, Median, Mode		Of all culture-positive isolates, the time between date of initial culture growth to genotype reported back to DOH.
NAA Testing	Percent	WA/ PHSKC	Percent of pulmonary culture positive cases having had NAA testing completed
Sputum smear + cases with contacts elicited	Percent	NTIP	Percent of TB patients with positive acid-fast bacillus(AFB) sputum-smear results who have contacts elicited
Infected who Started LTBI Treatment	Percent	NTIP	Percent of contacts to sputum AFB smear-positive TB patients with newly diagnosed latent TB infection (LTBI) who start treatment

Class B1 Post-Arrival Screening	Percent	WA	Percent of class B1 refugees and immigrants diagnosed with active TB in the U.S. who did not complete a post-arrival TB screening.
Class B1 Diagnosed with TB Post-Arrival	Percent	WA	Percent of Class B1 refugees and immigrants diagnosed with active TB in the U.S.
Class B1 Time to TB Diagnosis	Mean, Median Mode	WA	The time between arrival in the U.S. to the diagnosis of TB in the U.S.

National Program Objectives

The national TB program objectives reflect the national priorities for TB control in the United States. In 2006, a team representing TB programs and the Division of Tuberculosis Elimination (DTBE) selected 15 high-priority TB program objective categories. The program objective categories are:

1. Completion of treatment
2. TB case rates (in populations: U.S.-born persons, foreign-born persons, U.S.-born non-Hispanic blacks, and children younger than 5 years of age)
3. Contact investigations
4. Laboratory reporting
5. Treatment initiation
6. Sputum culture conversion
7. Data reporting (Report of Verified Case of Tuberculosis [RVCT], the Aggregate Reports for Tuberculosis Program Evaluation [ARPEs], and the Electronic Disease Notification [EDN] system)
8. Recommended initial therapy
9. Universal genotyping
10. Known HIV status
11. Evaluation of immigrants and refugees
12. Sputum culture reporting
13. Program evaluation
14. Human resource development plan
15. TB training focal points

TB programs funded through cooperative agreements will be expected to report on their progress toward achieving all 15 national TB program objective categories starting in 2010. These objectives can be found at http://www.cdc.gov/tb/publications/factsheets/statistics/NTIP.htm.

In addition to the national program objectives listed above, the CDC has two goals (listed below) that do not have national program objectives established at this time. Specific objectives relating to these two goals will be established in the future.

1. National Goal: Increase the percentage of immigrants and refugees designated as Class A, B1, or B2 who are appropriately evaluated and treated.

2. National Goal: For jurisdictions with greater than 50 reported cases of TB occurring annually in U.S.-born African Americans, decrease the case rate.

National Standards & Recommendations

Program standards are what the stakeholders of the TB program would consider to be "reasonable expectations" for the program. For TB, standards have been established by nationally accepted authorities, such as the American Thoracic Society (ATS), the Infectious Diseases Society of America (IDSA), and the CDC, and generally recognized TB control experts, such as the National Tuberculosis Nurse Coalition (NTNC) and the National Tuberculosis Controllers Association (NTCA). Many state programs, and some local TB control programs, have established their own standards and objectives for case management.[3] In 2011, the NTCA revised its Tuberculosis Nursing manual which will contain the most current program, structural and patient care standards that the NTCA recommends. Copies can be ordered from the NTCA at http://tbcontrollers.org.

The standards of care for the medical treatment and control of TB are published jointly by the ATS, IDSA, and CDC. These standards should be available for reference by each TB staff member.

The standards are included in the following guidelines:

- ATS, CDC, IDSA. "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America" (*MMWR* 2005;54[No. RR-12]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5412.pdf .
- ATS, CDC, IDSA. "Diagnostic Standards and Classification of Tuberculosis in Adults and Children" (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: http://www.cdc.gov/tb/publications/PDF/1376.pdf .
- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC, NTCA. "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC" (*MMWR* 2005;54 [No. RR-15]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf .
- CDC. "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf .
- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .

For additional guidelines, see the Division of Tuberculosis Elimination's "TB Guidelines" Web page (Division of Tuberculosis Elimination Web site; accessed December 12, 2011). Available at: http://www.cdc.gov/tb/publications/guidelines/default.htm.

Roles, Responsibilities, and Contact Information

Washington State Tuberculosis Services Staff

TABLE 3: WASHINGTON STATE TUBERCULOSIS ROLES, RESPONSIBILITIES AND CONTACT INFORMATION

Roles and Responsibilities	Contact Information
Role and Responsibilities of Washington State Tuberculosis Medical Consultant The Washington State Tuberculosis Services Medical Consultant provides a liaison for health care providers, particularly physicians treating patients with tuberculosis, and to educate them in matters related to diagnosis, treatment and case management of tuberculosis patients. Participate in seminars and workshops designed to educate health care providers on tuberculosis related issues; review medical records; provide consultation on interstate issues and policy development related to local health jurisdiction guidelines for treatment and control of tuberculosis; provide analysis of statewide genotyping database.	Scott Lindquist, MD, MPH Washington State Tuberculosis Services Medical Consultant Tel: 206-718-2664 E-mail: scott.lindquist@kitsappublichealth.org • TB Consultation Form
Role and Responsibilities of Washington State Program Manager	Washington State Tuberculosis Services Program Manager PO Box 47837 Olympia, WA 98504 Tel: 360-236-3443 Fax: 360-236-3405 Email: tbservices@doh.wa.gov

Roles and Responsibilities	Contact Information
Role and Responsibilities of Washington State Tuberculosis Controller Establishes short and long range program goals for prevention of infection and controlling disease; Assists in directing the planning, implementation and evaluation of program activities/special projects develops program policies, procedures and standards; provides oversight of preparation, allocation and monitoring of program resources and budget; collaborates with the TB Services Medical Consultant; supervises the maintenance of appropriate records and data collection systems and responds to inquiries regarding interpreting state TB laws and regulations. Provides direct consultation and technical assistance to local health jurisdictions (LHJ), schools, clinics, long-term care facilities, correctional facilities, homeless shelters, and other public and private agencies regarding TB policies and procedures.	Washington State Tuberculosis Services TB Controller PO Box 47837 Olympia, WA 98504 Tel: 360-236-3443 Fax: 360-236-3405 Email: tbservices@doh.wa.gov
Role and Responsibilities of Washington State Tuberculosis Services Nurse Consultant Advises personnel in local health jurisdictions, schools, clinics, long-term care facilities, correctional facilities, homeless shelters, and other public and private agencies within Washington State regarding TB programs, policy recommendations, practice standards for case management completion, contact investigation activities, treatment of latent TB infection, and distribution of nursing services. Participates in quarterly group reviews of case management activities, Cohort Review, by providing and discussing information such as treatment timing, nursing services-involved, practice standards, state and national objectives, and what is or is not contributing to successful management of TB cases Documents all TB cases reported, evaluating and forming recommendations regarding laboratory testing, treatment interruptions, medications, time to complete treatment.	Washington State Tuberculosis Services Nurse Consultant PO Box 47837 Olympia, WA 98504 Tel: 360-236-3443 Fax: 360-236-3405 Email: tbservices@doh.wa.gov

Roles and Responsibilities	Contact Information
Role and Responsibilities of Washington State Tuberculosis Services Support Staff As TB Services Support Staff, these positions support the program's mission by providing nursing care for patients with suspect or confirmed TB, conducting interviews and contact investigations of confirmed TB cases, providing community education for clients and healthcare providers, collecting/organizing TB case and treatment data and conducting various special projects	Washington State Tuberculosis Services Support Staff PO Box 47837 Olympia, WA 98504 Tel: 360-236-3443 Fax: 360-236-3405 Email: tbservices@doh.wa.gov

Local Health Jurisdictions and Private Medical Providers

TABLE 4: LOCAL HEALTH JURISDICTIONS' ROLES AND RESPONSIBILITIES

Local Health Jurisdictions	
Role and Responsibilities of Local Health Jurisdictions (WAC 246-170-031) 1. Each local health jurisdiction (LHJ) shall assure the provision of a comprehensive program for the prevention, treatment, and control of tuberculosis. Services shall include: **a.** Prevention and screening, with emphasis on screening of high risk populations; **b.** Diagnosis and monitoring, including laboratory and radiology; **c.** Individualized treatment planning consistent with American Thoracic Society/Centers for Disease Control and Prevention statements based on the least restrictive measures necessary to assure appropriate treatment; and **d.** Case management. 2. In the absence of third party reimbursement, the local health jurisdiction shall assure the provision of inpatient or outpatient care, including DOT/DOPT and case management. 3. Each local health jurisdiction shall maintain a register of all diagnosed or suspected cases of tuberculosis. In addition, each local health jurisdiction shall also maintain a register of individuals to whom that health department is providing preventive therapy. Quarterly status reports on suspected and diagnosed cases shall be furnished to the department of health tuberculosis control services.	4. A physician knowledgeable in the diagnosis and treatment of tuberculosis approved by the department shall be available to provide review of diagnoses, plans of management and, if appropriate, discharge from inpatient facilities. 5. Sufficient nursing, clerical, and other appropriate personnel shall be provided to furnish supervision of preventive and outpatient treatment, surveillance, suspect evaluation, epidemiologic investigation, and contact workup. For a list of local public health jurisdiction contacts, see http://www.doh.wa.gov/AboutUs/PublicHealthSystem/LocalHealthJurisdictions.aspx

TABLE 5: PRIVATE MEDICAL PROVIDERS' ROLES AND RESPONSIBILITIES

Private Medical Providers	
Role and Responsibilities of Private Medical Providers (WAC 246-101-105) 1. Notify the local health jurisdiction where the patient resides (in the event that patient residence cannot be determined, notify the local health jurisdiction where the medical providers practice) regarding: **a.** Cases or suspected cases of notifiable conditions specified as notifiable to local health jurisdictions in Table HC-1; **b.** Cases of conditions designated as notifiable by the local health officer within that health officer's jurisdiction; **c.** Outbreaks or suspected outbreaks of disease. These patterns include, but are not limited to, suspected or confirmed outbreaks of chickenpox, influenza, viral meningitis, nosocomial infection suspected due to contaminated food products or devices, or environmentally related disease; **d.** Known barriers which might impede or prevent compliance with orders for infection control or quarantine; and **e.** Name, address, and other pertinent information for any case, suspected case or carrier refusing to comply with prescribed infection control measures. 2. Notify the department of health of conditions designated as notifiable to the local health jurisdiction when: **a.** A local health jurisdiction is closed or representatives of the local health jurisdiction are unavailable at the time a case or suspected case of an immediately notifiable condition occurs; **b.** A local health jurisdiction is closed or representatives of the local health jurisdiction are unavailable at the time an outbreak or suspected outbreak of communicable disease occurs.	3. Notify the jurisdiction of pesticide poisoning that is fatal, causes hospitalization or occurs in a cluster. 4. Notify the jurisdiction as specified in Table HC-1 regarding cases of notifiable conditions specified as notifiable to the jurisdiction. 5. Assure that positive cultures and preliminary test results for notifiable conditions of specimens referred to laboratories outside of Washington for testing are correctly notified to the local health jurisdiction of the patient's residence or the jurisdiction as specified in Table Lab-1. This requirement can be satisfied by: **a.** Arranging for the referral laboratory to notify either the local health jurisdiction, the department, or both; or **b.** Forwarding the notification of the test result from the referral laboratory to the local health jurisdiction, the department, or both. 6. Cooperate with public health authorities during investigation of: **a.** Circumstances of a case or suspected case of a notifiable condition or other communicable disease; and **b.** An outbreak or suspected outbreak of disease. 7. Provide adequate and understandable instruction in disease control measures to each patient who has been diagnosed with a case of a communicable disease, and to contacts who may have been exposed to the disease. 8. Maintain responsibility for deciding date of discharge for hospitalized tuberculosis patients. 9. Notify the local health officer of intended discharge of tuberculosis patients in order to assure appropriate outpatient arrangements are arranged.

State Laboratory and Private Laboratories

TABLE 6: ROLE, RESPONSIBILITIES, AND CONTACT INFORMATION OF THE STATE LABORATORY AND PRIVATE LABORATORIES

Role and Responsibilities	Contact Information
State Laboratory The Washington State Department of Health's Public Health Laboratory (PHL) is an integral part of the DOH and the Public Health Improvement Plan (PHIP), the state's blueprint for improving the health status of Washington residents. As the state's primary reference laboratory, the PHL provides LHJs, hospitals, clinics and specialty laboratories with a wide range of services including identification, confirmation, susceptibility testing of pathogenic organisms, consultation and training in laboratory methodologies. The TB Unit receives and processes *Mycobacterium tuberculosis* (MTB) specimens five days a week. Microscopic results are provided within 24 hours of receipt except on weekends. The Acid-Fast Bacilli (AFB) positive results received by the PHL are entered into a TB computer database and reported within a day (by phone and fax) to submitting laboratories, physicians and to TB Control personnel. Using state of the art technology, the unit performs isolation and definitive identification on all mycobacterial isolates received by PHL. Drug susceptibility testing is also routinely performed on all first time MTB isolates and on isolates from patients whose symptoms suggest they are not responding to primary drugs. As a reference laboratory, the TB Unit also functions to help other laboratories improve their capabilities and services.	Washington State Department of Health Public Health Laboratory Street/Mailing address: 1610 NE 150th ST Shoreline, WA 98155 (King County) http://www.doh.wa.gov/PublicHealthandHealthcareProviders/PublicHealthLaboratories.aspx TB Lab Supervisor: 206-418-5474 TB Lab Lead: 206-418-5473
Private Laboratories Laboratories on this list provide primary specimen smear and culture testing for mycobacteria. Most refer isolates either to a Core Lab (reference Lab) or to the Washington State Department of Health Public Health Laboratories for identification and susceptibility testing.	For information on private laboratories see Laboratory Services Contact Information in the Laboratory section of the manual (10.4)

Resources and References

Resources

- CDC. "Framework for Program Evaluation in Public Health" (*MMWR* 1999;48[No. RR-11]). Available at: ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr4811.pdf.
- Division of Tuberculosis Elimination. *A Guide to Developing a TB Program Evaluation Plan* (Division of Tuberculosis Elimination Web site; accessed November 1, 2006). Available at: http://www.cdc.gov/tb/programs/evaluation/guide.htm.
- Division of Tuberculosis Elimination. *Understanding the TB Cohort Review Process: Instruction Guide* (Division of Tuberculosis Elimination Web site; accessed November 1, 2006). Available at: http://www.cdc.gov/tb/publications/guidestoolkits/cohort/default.htm.
- New Jersey Medical School National Tuberculosis Center. *Planning & Implementing the TB Case Management Conference: A Unique Opportunity for Networking, Peer Support and Ongoing Training* (Newark, NJ; 2004). Available at: http://www.umdnj.edu/globaltb/products/planning&implementing.htm.

References

[1] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):14.

[2] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):15.

[3] Division of Tuberculosis Elimination. National Center for HIV, AIDS and Tuberculosis Prevention, Centers for Disease Control and Prevention. *A Guide to Writing a TB Program Evaluation Plan* [Division of Tuberculosis Elimination Web site]:24. Available at: http://www.cdc.gov/tb/programs/evaluation/guide. Accessed December 12, 2011.

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BINATIONAL TB CARD (CureTB)

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Forms Used in this Section

- Binational Card Sample (Spanish)
- CureTB Brochure
- Binational Notification Form (CureTB)

Introduction

Purpose

Use this section to:

- Set up a Binational TB Card for persons traveling between Washington State and Mexico while receiving treatment for tuberculosis.

What is the public health problem?

- Tuberculosis (TB) is a significant problem among foreign-born persons in the United States. During 2010, foreign-born persons accounted for 74.9% of the 237 reported Washington cases; of these foreign-born persons, 35 (14.6%) were from Mexico.
- Some TB patients in Mexico do not have access to needed medications because they live in a remote area or are unable to afford the medications, which may lead to inadequate treatment regimens and multi-drug resistant (MDR) TB.
- About 461 TB cases receiving care in Washington between 2001-2010 originated from Mexico.
- Approximately 1 million persons cross the U.S.-Mexico border daily; an estimated 2.7 million persons from Mexico and Central America live in the United States without documentation of citizenship or visas.
- Reducing TB rates along the border and reducing disparities in TB disease treatment depend on finding and treating persons with or at risk for TB disease on both sides of the border.

What has CDC and its partners accomplished?

- The Centers for Disease Control and Prevention (CDC) works closely with the World Health Organization (WHO), the Pan American Health Organization (PAHO), the Mexican National TB Program, the U.S.-Mexico Border Health Commission and the four U.S. border states of California, Arizona, New Mexico and Texas to address the significant TB problem that exists along the 2,000-mile long-border. Specifically, CDC provided resources to assist Texas, Arizona and California in establishing binational health projects.
- The Washington State Department of Health Tuberculosis (TB) Program has collaborated on a project (2001) called the Binational TB Health Card Project with other partners across the nation, including the Centers for Disease Control and Prevention (CDC), Mexico, and U.S. border states including New Mexico, Texas, Arizona, California.

- TB patients have frequent crossings between the United States and Mexico, which complicate TB treatment. The goals of this project are to ensure continuity of care and assure that patients who have TB complete appropriate treatment

Policy

The Washington State TB Program is responsible for coordinating the process of referring patients traveling between Washington and Mexico to the CureTB: Binational TB Referral Program.

- TB patients who start care in Washington State will be given a card. If they leave for Mexico during the course of therapy, they will be referred to a provider in Mexico or, if leaving without notification of the local health jurisdiction (LHJ), are advised to call the 1-800 number on the card to find a health clinic to continue their treatment in Mexico. The card includes toll-free numbers in the United States and Mexico, a unique card number, the site where the patient first received TB care, treatment start date, treatment regimen, and whether the patient received directly observed therapy.
- Patients who start TB therapy in Mexico will have a card issued to them in Mexico. If they leave for the United States, Washington State will be notified of this patient by CureTB to assure that the patient continues to receive and complete therapy.

  Persons eligible for this card include anyone who:

  - Has active TB
  - Is a TB suspect at risk of being deported
  - Is Mexico-born
  - Is expected to travel to Mexico while on TB therapy (such as a migrant worker)
  - Has recently arrived from Mexico with drug therapy started in Mexico
  - Works in the United States and lives in Mexico

What Does CureTB do?

- Referral and follow-up of suspected and verified tuberculosis cases
- Referral/notification of contacts
- Referrals for source case finding
- Past history requests

What Does CureTB not do?

- Does not provide medications
- Does not provide direct services to patients (medical consultation, laboratory, transportation)
- Does not ship materials or medications to patients

Types of Referrals

- **Tuberculosis Cases and Suspects** - Patients with verified tuberculosis are referred to local health jurisdictions in the US or Mexico for initiation or continuation of treatment and follow-up. Patients suspected of active tuberculosis are referred for additional evaluation and/or for initiation/continuation of treatment.
- **Notification of Contacts** - Contacts to verified, infectious cases and to patients in whom there is high suspicion of infectiousness are notified to the local health jurisdictions where they reside in the US or Mexico.
- **Source Case Finding** - Requests for the search of an active case who may have infected patients currently under investigation for tuberculosis are submitted to local health jurisdictions in the US or Mexico.
- **Past History Requests** - Requests for patients' past medical histories pertaining to tuberculosis are submitted to the local health jurisdictions where they resided in the US or Mexico.
- **LTBI Treatment** - Treatment for Latent TB Infection

Issuing a Binational Card

A Binational card is issued to:

- TB cases (both suspect and counted), in all local health jurisdiction (LHJs), that have started TB medications and might return to or travel from Mexico during their treatment.

Local Health Jurisdiction Responsibilities

Local Health Jurisdictions with TB cases who were born in Mexico and travel to/from Mexico:

- Call/FAX information for Binational Card to DOH Nurse Consultant
- Mail/deliver Binational Card to patient when received
- Notify DOH via the Binational TB Notification form when patient leaves the country
- DOH will fax Binational TB Notification form to CureTB

Role of DOH TB Nurse Consultant

- Discuss with LHJ TB Case Manager the potential need for Binational Card on each newly reported case born in Mexico with history of travel to/from Mexico
- If need for Binational Card identified, obtain the following information from LHJ TB Case Manager:
    - Full name of patient and date of birth
    - Local home/cell phone number
    - Contact name, address (town, county), phone number in Mexico for someone who knows where the patient will likely stay or visit. Completed CureTB form needs to include address and phone number (if possible) in Mexico. If no address or phone number, then do NOT send Binational form to CureTB, as they cannot provide assistance on any case if this data is missing.
    - Enter Binational Card unique number onto Binational log database and note criteria for providing the card
    - Enter into PHIMS TB database Comment Section: Binational card number, date of issue, Alien number if applicable
    - When patient moves to Mexico
    - If time allows, provide CureTB with Binational information PRIOR to patient's move, and include potential departure/arrival dates. FAX Binational Notification Referral Form to (619) 692-8020.
    - For all TB cases that have moved to Mexico contact CureTB to see if patient has been located 30 days after TB case has left the U.S and at anticipated date of treatment completion.
    - If CureTB report patient was never found in Mexico, leave case closed as "moved", but make a note in the PHIMS TB comment section that "patient unable to be located in Mexico"
    - When (if) CureTB provides a report that patient has completed medications in Mexico, update PHIMS TB that medications have been completed and change the reason for closure from "moved" to "completed" and note the number of weeks of DOT and weeks of self-administered medications
    - When (if) CureTB provides a report that patient had several months of medications but did not complete the treatment, place updated notes the comments section, as well as, the amount of time (weeks) the patient had of treatment.
    - CureTB often sends an updated/final report letter to DOH TB
    - Notify LHJ that patient has completed medications.

TB patients originating in Mexico and traveling to Washington State

- Cure TB will call the Washington State Department of Health TB Program
- The Nurse Consultant will contact the LHJ to share patient information and verify card number.
- When the patient completes therapy, the LHJ will enter the information into PHIMS TB to notify the Nurse Consultant and close the patient's case in Washington. The Nurse Consultant will send updated RVCT to CureTB.

Resources

- Binational Card Sample (in Spanish)
- CureTB Brochure
- Binational Notification Form
- Migrant Clinician's Network

For information on CureTB, visit www.curetb.org.

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Surveillance

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Forms Used in this Section

- Acknowledgement of TB Counseling (PHSKC)
- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Civil Detention Flowchart
- Clinic Record (SHD)
- Contact Investigation
- DOT Agreement (PHSKC)
- DOT Agreement (Virginia)
- Home Evaluation (SHD)
- Home Isolation Agreement (SHD)
- Interjurisdictional TB Notification
- Interjurisdictional TB Notification Follow-Up
- Laboratory Data Sheet
- RVCT Form (CDC)
- Public Health Directive (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)

Introduction

Purpose

Use this section to do the following:

- Understand the importance of surveillance in tuberculosis (TB) control and prevention.
- Report suspected and confirmed TB cases.
- Ensure you are using the required data collection forms.
- Understand how the web application for reporting TB (PHIMS TB) works.
- Understand how genotyping can assist TB control efforts.

Surveillance—the ongoing systematic collection, analysis, interpretation, and dissemination of data about a health-related event—is a critical component of successful TB control, providing essential information needed to do the following:

1. Determine TB patterns and trends of the disease.
2. Identify sentinel events, such as potential outbreaks, recent transmission, multidrug resistance, and deaths.
3. Identify high-risk populations and settings.
4. Establish priorities for control and prevention activities.
5. Strategically plan the use of limited resources.[1]

Surveillance data are also essential for quality-assurance purposes, program evaluation, and measurement of progress toward TB elimination.

State and local TB control programs should have the capability to monitor trends in TB disease and latent TB infection (LTBI) in populations at high risk, in order to detect new patterns of disease and possible outbreaks. Populations at high risk should be identified and targeted for active surveillance and prevention, including targeted testing and treatment of LTBI. The following populations have been demonstrated to be at risk for TB exposure, progression from exposure to disease, or both: children, foreign-born persons, human immunodeficiency virus (HIV)-infected persons, homeless persons, and detainees and prisoners. Surveillance and surveys from throughout the United States indicate that certain epidemiologic patterns of TB are consistently observed among these populations, suggesting that the recommended control measures are generalizable. State and local surveillance data should be analyzed to determine additional high-risk population groups.

In addition to providing the epidemiologic profile of TB in a given jurisdiction, state and local surveillance are essential to national TB surveillance.[2] Data for the national TB surveillance system are reported by state health departments in accordance with standard TB case definition and case-report formats. The Report of Verified Case of Tuberculosis (RVCT) forms (both the CDC version and the Washington State electronic PHIMS TB edition) are designed to collect information on cases of TB. The Centers for Disease Control and Prevention's (CDC's) national TB surveillance system publishes epidemiologic analyses of reported TB cases in the United States.[3]

Reporting of new cases is essential for surveillance purposes.[4]

Surveillance in TB Control Activities

Case detection: Case reporting to the jurisdictional public health agency is done for surveillance purposes and for facilitating a treatment plan and case management services.[5]

For more information on case reporting, see the "Reporting Tuberculosis" topic in this section of the manual (**2.8**).

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Outbreak detection: Surveillance data should be routinely reviewed to determine if there is an increase in the expected number of TB cases, one of the criteria for determining if an outbreak is occurring. For an increase in the expected number of TB cases to be identified, the local epidemiology of TB should be understood. Detection of a TB outbreak in an area in which prevalence is low might depend on a combination of factors, including recognition of sentinel events, routine genotype cluster analysis of surveillance data, and analysis of *Mycobacterium tuberculosis* drug-resistance and genotyping patterns.[6] Genotyping data should routinely be reviewed because genotype clusters also may indicate an outbreak. Prompt identification of potential outbreaks and rapid responses are necessary to limit further TB transmission. When an outbreak is identified, short-term investigation activities should follow the same principles as those for the epidemiologic part of the contact investigation (i.e., identifying the infectious period, settings, risk groups, mode of transmission, contact identification, and follow-up). However, long-term activities require continued active surveillance.

For more information on outbreak investigations, see the "Outbreak Investigation" topic in the Contact Investigation section of the manual (**9.45**).

Contact investigation: Collecting, analyzing, interpreting, and disseminating data on contacts and contact investigations are necessary for prioritizing the highest-risk contacts, to focus the use of resources, in accordance with national guidelines. Although surveillance of individual contacts to TB cases is not conducted in the United States, the CDC collects aggregate data from state and local TB programs through the *Aggregate Report for Program Evaluation (ARPE).* Routine collection and review of this data can provide the basis for evaluation of contact investigations for TB control programs.[7]

For more information on surveillance in contact investigations, see the Contact Investigation section of the manual (**9.1**).

Targeted testing: Review and interpretation of surveillance data inform targeted testing policies and strategies. Targeted testing is intended to identify persons other than TB contacts who have an increased risk for acquiring TB and to offer such persons diagnostic testing for *M. tuberculosis* infection and treatment, if indicated, in order to prevent subsequent progression to TB disease. Targeted testing and treatment of LTBI are best accomplished through cost-effective programs aimed at patients and populations identified on the basis of local surveillance data as being at increased risk for TB.[8]

For more information on surveillance and targeted testing, see "Targeted Testing for Latent Tuberculosis Infection" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

Treatment of LTBI: Surveillance of persons with LTBI does not routinely occur in the United States. However, the CDC has a National Surveillance System for Severe Adverse Events Associated with Treatment for Latent Tuberculosis Infection. This system collects data on patients who received at least one dose of drug therapy for treatment of LTBI resulting in hospitalization or death. Healthcare providers are encouraged to report such events to the CDC's Division of Tuberculosis Elimination by calling 404-639-8401. Surveillance of these events will provide data to evaluate the safety of treatment regimens recommended in current guidelines.[9]

For more information on surveillance and targeted testing, see the Targeted Testing section. For more information on updated LTBI treatment recommendations, see the CDC's "Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection—United States, 2003" (*MMWR* 2003;52[31];735–739) at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm .

Policy

Data collection and reporting on TB should be done in accordance with Washington State laws and regulations. Reporting and recordkeeping requirements are covered in this section.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction section of the manual (**1.16**).

For more information on confidentiality and the Health Insurance Portability and Accountability Act (HIPAA), see the Confidentiality section of the manual (**12.3**).

Laws and Rules

Washington State laws and rules on tuberculosis (TB) are located in the Washington Administrative Code (WAC) and the Revised Code of Washington (RCW).

In the WAC, see Chapter 246-170 (Tuberculosis Control) in Title 246 (Department of Health) at http://apps.leg.wa.gov/WAC/default.aspx?cite=246-170

In the RCW, see chapter 70.28 (Control of Tuberculosis) at http://apps.leg.wa.gov/RCW/default.aspx?cite=70.28

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Contact Washington State TB Services at 360-236-3443 for assistance with interpreting Washington State laws and rules regarding TB control.

Tuberculosis Classification System

The system for classifying tuberculosis (TB) is based on how the infection and disease develop in the body. Use this classification system to help track the status of TB in your patients and to allow comparison with other reporting areas.

TABLE 1: TUBERCULOSIS CLASSIFICATION SYSTEM[10]

Class	Type	Description
0	• No TB exposure • Not infected	• No history of TB exposure and no evidence of M.tuberculosis infection or disease • Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	• TB exposure • No evidence of infection	• History of exposure to M. tuberculosis • Negative reaction to the TST or IGRA (given at least 8-10 weeks after exposure)
2	• TB infection • No TB disease	• Positive reaction to the TST or IGRA • Negative bacteriological studies (smear and cultures) • No bacteriological or radiographic evidence of active TB disease
3	• TB Clinically active	• Positive culture for *M. tuberculosis* • Positive reaction to TST or IGRA, plus clinical, bacteriological, or radiographic evidence of current active TB
4	• Previous TB disease (not clinically active)	• May have past medical history of TB disease • Abnormal but stable radiographic findings • Positive reaction to the TST or IGRA • Negative bacteriologic studies (smear and cultures) And • No clinical or radiographic evidence of current active TB disease
5	• TB suspected	• Signs and symptoms of active TB disease, but medical evaluation not complete

Source: Adapted from: CDC. Classification system. In: Chapter 2: transmission and pathogenesis. *Core Curriculum on Tuberculosis (2011)* [Division of Tuberculosis Elimination Web site]. Available at: http://www.cdc.gov/tb/education/corecurr/index.htm .

Reporting Tuberculosis

Detecting and reporting suspected cases of tuberculosis (TB) is the key step in stopping transmission of *Mycobacterium tuberculosis* because it leads to prompt initiation of effective multiple-drug treatment, which rapidly reduces infectiousness. The Centers for Disease Control and Prevention (CDC) reports that delays in reporting cases of pulmonary TB are one of the major challenges to successful control of TB.[11] As one of the strategies to achieve the goal of reduction of TB morbidity and mortality, the CDC recommends immediate reporting of a suspected or confirmed case of TB to the jurisdictional health agency.[12] Also, by Washington State law and regulation, a case of TB disease in the United States must be reported to the local public health jurisdiction (**2.10**).

When reporting TB, keep the following definitions in mind:

- **Case:** An episode of TB disease in a person meeting the laboratory or clinical criteria for TB, as defined in the document "Case Definitions for Infectious Conditions Under Public Health Surveillance."[13] These criteria are listed below in Table 2.[14]
- **Suspect:** A person for whom there is a high index of suspicion for active TB (e.g., a known contact to an active TB case or a person with signs or symptoms consistent with TB) who is currently under evaluation for TB disease.[15]
- **Confirmed:** A case that meets the clinical case definition or is laboratory confirmed, as described below in Table 2.[16]

TABLE 2: CASE DEFINITIONS[17]

Clinical Case Definition	Laboratory Criteria for Diagnosis
A clinical case that meets all of the following criteria: • A positive tuberculin skin test or IGRA • Other signs and symptoms compatible with tuberculosis (e.g., an abnormal, unstable [i.e., worsening or improving] chest radiograph, or clinical evidence of current disease) • Treatment with 2 or more antituberculosis medications • Completed diagnostic evaluation	A case is laboratory confirmed when it meets one of the following criteria: • Isolation of *Mycobacterium tuberculosis from* a clinical specimen* • Demonstration of *M. tuberculosis* from a clinical specimen by nucleic acid amplification (NAA) test† • Demonstration of acid-fast bacilli (AFB) in a clinical specimen when a culture has not been or cannot be obtained

* Use of rapid identification techniques for *M. tuberculosis* (e.g., deoxyribonucleic acid [DNA] probes and mycolic acids high-pressure liquid chromatography performed on a culture from a clinical specimen) is acceptable under this criterion.

† NAA tests must be accompanied by culture for mycobacteria species. However, for surveillance purposes, the CDC will accept results obtained from NAA tests approved by the Food and Drug Administration and used according to the approved product labeling on the package insert.

Source: Adapted from: CDC. Case definitions for infectious conditions under public health surveillance. *MMWR* 1997;46(No. RR-10):40–41.

Suspect pulmonary TB and initiate a diagnostic investigation when the historic features, signs, symptoms, and radiographic findings of TB are evident among adults. TB should be suspected in any patient who has a persistent cough for over two to three weeks, or other indicative signs and symptoms.[18]

For more information on suspected pulmonary TB, see the Diagnosis of Tuberculosis Disease section of the manual (**4.1**).

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Mandatory and timely case reporting from community sources (e.g., providers, laboratories, hospitals, and pharmacies) should be enforced and evaluated regularly. Reporting enables the TB control program to take action at local, state, and national levels and to understand the magnitude and distribution of the TB problem.[19]

Prompt reporting (prior to culture confirmation) allows the state and local public health jurisdiction to do the following quickly:

- Verify diagnosis
- Assign a case manager and coordinate treatment
- Determine if an outbreak is occurring
- Control the spread of TB[20]

Failure to report cases threatens public health because it may result in the adverse outcome of a patient's treatment or delayed contact investigation of an infectious case.[21]

Reporting Confirmed Cases of Tuberculosis

Report confirmed cases of TB using the information in Table 3.

TABLE 3: WHEN TO REPORT TUBERCULOSIS

What Condition/ Test Result	Who Reports	When to Report	How to Report
Confirmed cases of tuberculosis (TB) disease This includes pulmonary and extrapulmonary cases.	Healthcare Providers or Anyone providing treatment to the confirmed case Note: The attending physician or other healthcare provider must report even if the laboratory is also reporting the test results.	Report Immediately	Notify the local health jurisdiction in the county of the patient's residence. For a list of local public health jurisdictions in Washington State and their contact information, refer to this document: http://www.doh.wa.gov/AboutUs/PublicHealthSystem/LocalHealthJurisdictions.aspx. WAC 246-101-101 Notifiable Conditions and the health care provider Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx
Confirmed cases of tuberculosis (TB) disease This includes pulmonary and extrapulmonary cases.	Hospitals and other similar private or public institutions Note: The attending physician or other healthcare provider must report even if the laboratory is also reporting the test results.	Report Immediately	Notify the local health jurisdiction in the county of the patient's residence. For a list of local public health jurisdictions in Washington State and their contact information, refer to this document: http://www.doh.wa.gov/AboutUs/PublicHealthSystem/LocalHealthJurisdictions.aspx. WAC 246-101-301 Notifiable Conditions and health care facilities Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx
Mycobacterium tuberculosis	Laboratories	Report culture within 2 business days	Notify the Department of Health DOH TB Reporting Line: 360-236-3397 Or DOH TB Reporting Fax Line: 360-236-3405 WAC 246-101-201

What Condition/ Test Result	Who Reports	When to Report	How to Report
			Notifiable Conditions and laboratories Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx
Mycobacterium tuberculosis (antibiotic sensitivity for first isolates)	Laboratories	Report within 2 business days	Notify the Department of Health DOH TB Reporting Phone Line: 360-236-3397 Or DOH TB Reporting Fax Line: 360-236-3405 WAC 246-101-201 Notifiable Conditions and laboratories Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Healthcare Providers

Responsibilities of Private Medical Providers (WAC 246-101-105)

1. Notify the local health jurisdiction where the patient resides (in the event that patient residence cannot be determined, notify the local health jurisdiction where the health care providers practice) regarding:
   - **a.** Cases or suspected cases of notifiable conditions specified as notifiable to local health jurisdiction in Table HC-1;
   - **b.** Cases of conditions designated as notifiable by the local health officer within that health officer's jurisdiction;
   - **c.** Outbreaks or suspected outbreaks of disease. These patterns include, but are not limited to, suspected or confirmed outbreaks of chickenpox, influenza, viral meningitis, nosocomial infection suspected due to contaminated food products or devices, or environmentally related disease;
   - **d.** Known barriers which might impede or prevent compliance with orders for infection control or quarantine; and
   - **e.** Name, address, and other pertinent information for any case, suspected case or carrier refusing to comply with prescribed infection control measures.

2. Notify the department of health of conditions designated as notifiable to the local health jurisdiction when:
   a. A local health jurisdiction is closed or representatives of the local health jurisdiction are unavailable at the time a case or suspected case of an immediately notifiable condition occurs;
   b. A local health jurisdiction is closed or representatives of the local health jurisdiction are unavailable at the time an outbreak or suspected outbreak of communicable disease occurs.
3. Notify the jurisdiction of pesticide poisoning that is fatal, causes hospitalization or occurs in a cluster.
4. Notify the jurisdiction as specified in Table HC-1 regarding cases of notifiable conditions specified as notifiable to the jurisdiction.
5. Assure that positive cultures and preliminary test results for notifiable conditions of specimens referred to laboratories outside of Washington for testing are correctly notified to the local health jurisdiction of the patient's residence or the jurisdiction as specified in Table Lab-1. This requirement can be satisfied by:
   a. Arranging for the referral laboratory to notify either the local health jurisdiction, the department, or both; or
   b. Forwarding the notification of the test result from the referral laboratory to the local health jurisdiction, the department, or both.
6. Cooperate with public health authorities during investigation of:
   a. Circumstances of a case or suspected case of a notifiable condition or other communicable disease; and
   b. An outbreak or suspected outbreak of disease.
7. Provide adequate and understandable instruction in disease control measures to each patient who has been diagnosed with a case of a communicable disease, and to contacts who may have been exposed to the disease.
8. Maintain responsibility for deciding date of discharge for hospitalized tuberculosis patients.
9. Notify the local health officer of intended discharge of tuberculosis patients in order to assure appropriate outpatient arrangements are arranged.

Laboratories

Responsibilities of Laboratories (WAC 246-101-201)

This section describes the conditions about which Washington's laboratories must notify public health authorities of on a statewide basis. The board finds that the conditions in Table Lab-1 are notifiable for the prevention and control of communicable and noninfectious diseases and conditions in Washington. The board also finds that submission of specimens for many of these conditions will further prevent the spread of disease. Laboratory directors must notify public health authorities of positive cultures and preliminary test results as individual case reports and provide specimen submissions using procedures described throughout this chapter. Local health officers may require additional conditions to be notifiable within the local health officer's jurisdiction.

WAC 246-101-205, 246-101-210, 246-101-215, 246-101-220, 246-101-225, and 246-101-230 also include requirements for how notifications and specimen submissions are made, when they are made, the content of these notifications and specimen submissions, and how information regarding notifiable conditions cases must be handled and may be disclosed.

Required Reports from Local Public Health Jurisdictions to Washington State Tuberculosis Services

Local public health jurisdictions are required to complete and submit the reports listed in Table 4 to Washington State TB Services at the Washington State Department of Health.

Contact Investigation forms can be faxed to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

TABLE 4: REQUIRED REPORTS

Report Title	When Due
• PHIMS TB	Within 7 days of receipt of confirmed/suspect case notification by the local health jurisdiction
• PHIMS TB	When there are changes to the TB Case Report and when the TB case is closed (the end of treatment)
• Contact Investigation	At these milestones during a contact investigation of exposure to pulmonary TB: • Upon completion of initial tuberculin skin testing or IGRA testing of contacts (usually 10-15 days) • Upon completion of retests of contacts • Upon contacts' completion of therapy for latent tuberculosis infection • Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks For recommended time frames of tasks in contact investigations, refer to the "Time Frames for Contact Investigation" topic in the Contact Investigation section of the manual (9.16).

To download forms for the above required reports, go to the **FORMS** section of the manual.

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at
http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at
http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Data Collection Forms

It is recommended that the following standardized forms (or similar forms developed by local health jurisdictions) be completed and placed in the patient's chart and/or a contact investigation file if and when the related activities are performed.

TABLE 5: RECOMMENDED FORMS FOR A TUBERCULOSIS PATIENT'S CHART

Chart of a Patient on Treatment for Tuberculosis Disease	
Tuberculosis (TB) Disease Treatment/Case Management • RVCT Form (printed version from PHIMS) • Dot Agreement (Virginia) • Home Isolation Agreement (SHD) • Home Evaluation (SHD) • Laboratory Data Sheet • Clinic Record (SHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart	Transfer Notifications • Interjurisdictional TB Notification • Interjurisdictional TB Notification Follow-Up
Chart of a Patient on Treatment for Latent Tuberculosis Infection	
Latent Tuberculosis Infection (LTBI) Treatment • Clinic Record (SHD)	If on Directly Observed Therapy • DOT Agreement (Virginia) • DOT Agreement (PHSKC) Transfer Notifications • Interjurisdictional TB Notification • Interjurisdictional TB Notification Follow-Up
File for a Contact Investigation	
• Contact Investigation • Contact Investigation Instructions	

To download the above recommended forms, go to the **FORMS** section of the manual.

PHIMS TB (Public Health Issue Management System)

To carry out mandatory community public health responsibilities, the state TB control program maintains a web-based reporting system where up-to-date information on all current clinically active and suspected TB cases in the community can be entered and accessed. The PHIMS TB program should ensure that laboratory data, including all initial positive diagnostic tests, are promptly reported to the Department of Health by the local health jurisdictions (LHJs). Follow-up tests, including data on sputum culture conversion and drug susceptibility testing of clinical isolates, should also be promptly reported so any needed modifications in management can be made. Aggregate program data should be analyzed, interpreted, and made available to the healthcare community and to community groups and organizations with specific interests in public health. Providing this information supports education and advocacy and facilitates collaboration in the planning process.

- Local Health Jurisdictions will use PHIMS TB to:
  - Report TB suspects and cases to DOH
  - Enter current clinical information and updates
  - View case summary reports and exports
  - Document quality assurance and cohort data

For more information on the TB PHIMS program, see the PHIMS TB User Guide at:

http://www.doh.wa.gov/Portals/1/Documents/Pubs/343-099-PHIMSTBUserManual.pdf

Genotyping

Genotyping is a useful tool for studying the pathogenesis, epidemiology, and transmission of *Mycobacterium tuberculosis. M. tuberculosis* genotyping refers to laboratory procedures developed to identify *M. tuberculosis* isolates that are identical in specific parts of the genome (of similar strain types).

Genotyping is based on an analysis of deoxyribonucleic acid (DNA). Mycobacteria reproduce by binary fission, which means that in almost all cases each new bacillus has identical DNA, just as human identical twins are genetically identical to each other. However, changes in the DNA occur spontaneously at low frequency. Over time, these changes, known as DNA mutations, have accumulated to produce the diversity of *M. tuberculosis* strains currently circulating in the world.

The diversity of strain provides a means to identify instances of recent transmission of tuberculosis (TB) as well as the chains of transmission that occur among persons with TB. This diversity also helps to elucidate the patterns and dynamics of TB transmission. When a person with TB improves but then becomes ill again, this diversity can differentiate reactivation with the same strain of *M. tuberculosis* from reinfection with a different strain. Genotyping can also be used to identify false-positive cultures.

Advances in DNA analytic methods have made it possible for TB programs to obtain rapid and reliable genotyping results. These advances include the following:

- The determination of the complete DNA sequence of *M. tuberculosis* in 1998
- The development of IS6110-based restriction fragment length polymorphism (RFLP) genotyping, which provided a discriminatory typing method and led to a standardized system for genotyping *M. tuberculosis* isolates
- The development of two new methods, spoligotyping and mycobacterial interspersed repetitive units (MIRU) analysis, which are based on polymerase chain reaction (PCR) and provide much more rapid results than RFLP analysis[22]

The addition of genotype information to the pool of information generated by surveillance data and data collected through epidemiologic investigation allow confirmation of suspected transmission. A potential outbreak should be suspected whenever there is more than one case of TB whose isolate has the same genotype (genotype cluster). Further investigation that includes review of surveillance data, chart review, and reinterview of TB cases may refute or confirm the epidemiologic connection between more than one TB case. In some instances, a genotype cluster reflects a false-positive culture that may be a result of laboratory cross-contamination. Routine review of genotyping data, along with epidemiologic, clinical, and laboratory data, may identify patients who are wrongly classified as TB patients and should be further investigated.

The Washington State TB Services reviews genotyping data to check for any matches. Upon identification of a match, Washington State TB Services telephones the local health jurisdictions managing the case to discuss what further steps should be taken.

For more information on genotyping, see the National Tuberculosis Controllers Association/Centers for Disease Control and Prevention Advisory Group on Tuberculosis Genotyping's *Guide to the Application of Genotyping to Tuberculosis Prevention and Control* (2004) at http://www.cdc.gov/tb/programs/genotyping/manual.htm .

All *M. tuberculosis* cultures originating at the Washington State Public Health Laboratory are automatically submitted to a national genotyping laboratory for genotyping analysis.

For more information on Restriction Fragment Length Polymorphism (RFLP) see http://www.cdc.gov/tb/programs/genotyping/Chap5/5_Developing_3c_RFLP.htm.

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DOH 343-071 June 2012
For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

B Notifications

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Introduction

Purpose

Use this section to do the following:

- Follow up on B1, B2 and B3 notifications and
- Evaluate and treat immigrants, refugees and asylees with B1, B2 and B3 notifications.

B1/B2/B3 notifications are sent by the Centers for Disease Control and Prevention (CDC) to the Washington State Tuberculosis (TB) Services as follow-up to overseas screening mandated by US immigration law. The CDC and the Advisory Council for the Elimination of Tuberculosis (ACET) recommend screening high-risk populations for TB, including recent arrivals from areas of the world with a high prevalence of TB. Therefore, screening of foreign-born persons is a public health priority.[1] On the basis of its very high success rate of detecting TB cases, domestic follow-up evaluation of immigrants, refugees and asylees with Class B1, B2 and B3 TB notification status should be given highest priority by all TB control programs.[2] Legal immigrants, refugees, and asylees with Class B1,B2 and B3 TB notification status are also a high-priority subpopulation for screening for latent TB infection (LTBI). [2]

The purpose of the medical examination is to identify, for the Department of State and the US Citizenship and Immigration service, applicants with medical conditions of public health concern.[3]

Not all foreign-born persons who enter the United States go through the same official channels or through the screening process.[2] For a summary of which groups of foreign-born persons that are screened, refer to Table 1.

TABLE 1: NUMBERS OF FOREIGN-BORN PERSONS WHO ENTERED THE UNITED STATES, BY IMMIGRATION CATEGORY, 2002

Category	Number	Percentage of Total	Screening Required?
Immigrants are defined by the Office of Immigration Statistics (OIS) as persons legally admitted to the United States as permanent residents.	384,000	1.38%	Yes
Refugees and asylees, as defined by OIS, are persons admitted to the United States because they are unable or unwilling to return to their country of nationality due to persecution or a well-founded fear of persecution. Refugees apply for admission at an overseas facility and enter the United States only after their application is granted; asylees apply for admission when already in the United States or at a point of entry.	132,000	0.46%	Yes
Nonimmigrants are aliens granted temporary entry to the United States for a specific purpose (most common visa classifications for nonimmigrants are visitors for pleasure, visitors for business, temporary workers, and students).	27,907,000	98.18%	No
The foreign-born population, as defined by the Census Bureau, refers to all residents of the United States who were not US citizens at birth, regardless of their current legal or citizenship status.	28,423,000	100%	See above
Unauthorized immigrants (also referred to as illegal or undocumented immigrants) are foreign citizens illegally residing in the United States. They include both those who entered without inspection and those who violated the terms of a temporary admission without having gained either permanent resident status or temporary protection from removal.			

Sources: Congress of the United States, Congressional Budget Office. *A Description of the Immigrant Population*. Washington, DC: Congressional Budget Office; November 2004; and ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):46.

In Washington State, between 2008 and 2010, an average of 2,600 refugees arrived each year.[4]

Persons entering in the nonimmigrant category do not require pre-entry screening, but as a condition of entry, persons migrating as immigrants, refugees, and asylees are required to be screened outside of the United States for diseases of public health significance, including TB.[5] Applicants for immigration who plan to relocate permanently to the United States are required to have a medical evaluation prior to entering the country.

Immigrants coming from several countries with high rates of tuberculosis are being screened according to new 2007 guidelines, see http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html.

The new guidelines are also being implemented for other high tuberculosis incidence countries.

The following table displays applicants for U.S. immigration being screened according to the 2007 Technical Instructions for Tuberculosis Screening and Treatment by country, population, and start date as of January 23, 2009.

TABLE 2: APPLICANTS SCREENED ACCORDING TO 2007 TECHNICAL INSTRUCTIONS BY COUNTRY

Country	Population	Start date
Bangladesh	All applicants	June 15, 2011
Botswana	All applicants	March 3, 2008
Cambodia	All applicants	February 1, 2010
China	All applicants	July 1, 2009
Colombia	All applicants	August 15, 2011
Dominican Republic	All applicants	February 2, 2009
Egypt	All applicants	November 15, 2009
Ethiopia	Refugees (Eritreans)	March 10, 2009
	All applicants	April 1, 2009
Ghana	All applicants	October 1, 2010
Guatemala	All applicants	May 2, 2011
Haiti	All applicants	September 26, 2009
Hong Kong SAR	All applicants	November 3, 2008
India	All applicants	October 1, 2010
Japan	All applicants	June 1, 2009
Jordan	All applicants	April 5, 2009
Kenya	Refugees (includes Ethiopians, Somalis, and Sudanese)	January 1, 2008
	All applicants	April 1, 2009
Lesotho	All applicants	March 3, 2008
Macau SAR	All applicants	November 3, 2008
Malaysia	Refugees (Burmese)	January 1, 2009
Mexico	All applicants	October 1, 2007
Mozambique	All applicants	March 3, 2008
Namibia	All applicants	March 3, 2008
Nepal	Refugees (Bhutanese)	December 13, 2007
	All applicants	August 2, 2010
Nigeria	All applicants	October 1, 2010
Philippines	All applicants	October 1, 2007
South Africa	All applicants	March 3, 2008
South Korea	All applicants	May 2, 2011
Swaziland	All applicants	March 3, 2008
Taiwan	All applicants	April 1, 2009
Tanzania	Refugees (Burundian)	January 1, 2008
	All applicants	June 5, 2008
Thailand	Refugees (includes Burmese and Hmong refugees)	April 9, 2007
	All applicants	April 25, 2011
Turkey	All applicants	February 4, 2008
Uganda	All applicants	March 2, 2009
Vietnam	All applicants	February 1, 2008

Refer to http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-implememtation.html for current information.

All other applicants for U.S. immigration are still being screened according to the 1991 Tuberculosis Technical Instructions, available at http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/technical-instructions-panel-physicians.html.

Under the 1991 Guidelines, applicants who are identified as having abnormalities in their chest radiographs consistent with TB are classified according to the criteria in Table 3. An applicant whose chest radiograph is compatible with active TB, but whose sputum AFB smear results are negative, is classified as having Class B1 status and may enter the United States. If the chest radiograph is compatible with inactive TB, no sputum specimens are required, and the applicant may enter the country with Class B2 status. If abnormalities are present in a chest radiograph and sputum AFB smears are positive, the applicant must receive a Class A waiver before entry into the United States. Very few persons with A waivers enter the United States, so A waivers are not covered in these guidelines.

The Class B notification system continues follow-up on medical screenings of persons with B1 and B2 classifications after their arrival in the United States. Immigrants with a Class A waiver or with Class B1 or B2 status are identified at ports of entry to the United States by the US Citizenship and Immigration Services (USCIS) and reported to CDC's Division of Global Migration and Quarantine (DGMQ). The DGMQ notifies Washington State Department of Health TB Services of refugees, immigrants and asylees with TB classifications who are moving to their jurisdiction and need follow-up evaluations. Persons with a Class A waiver are required to report to the local jurisdictional public health agency for evaluation, or risk deportation. For persons with Class B1 and B2 status, however, the stipulated evaluation visits to the health agency are voluntary.[2]

TABLE 3: 1991 CLASSIFICATION OF IMMIGRANTS AND REFUGEES IN THE B NOTIFICATION PROGRAM

Immigrant/ Refugee Classification	Overseas Chest Radiograph	Overseas Sputum Acid-Fast Bacilli Smears	Restrictions
A Waiver*	Abnormal, suggestive of active tuberculosis (TB) disease	Positive	May not enter the United States unless started on antituberculosis therapy with sputum smears converted to negative and: ▪ Apply for a waiver signed by the local health jurisdiction at their intended US destination (A Waiver) or ▪ Complete TB therapy overseas
B1	Abnormal, suggestive of	Negative	Instructed to voluntarily report to the local health jurisdiction in the United

	active TB disease		States for further medical evaluation within 30 days of arrival
B2	Abnormal, suggestive of inactive TB disease	Negative	Same as above
* Very few persons with A waivers enter the United States, so they are excluded from these guidelines.			

Source: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). Guidelines for the follow-up and assessment of persons with Class B1/B2 tuberculosis. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. September 1999:1. Available at: http://www.ctca.org/fileLibrary/file_54.pdf

The criteria for assigning screening categories in the new 2007 classification system are shown in Table 4.

TABLE 4: 2007 CLASSIFICATION SYSTEM

No TB Classification	Applicants with normal tuberculosis screening examinations.
Class A TB with waiver	All applicants who have tuberculosis disease and have been granted a waiver.
Class B1 TB, Pulmonary	**No treatment** • Applicants who have medical history, physical exam, HIV, or CXR findings suggestive of pulmonary tuberculosis but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis or can wait to have tuberculosis treatment started after immigration. **Completed treatment** • Applicants who were diagnosed with pulmonary tuberculosis and successfully completed directly observed therapy prior to immigration. The cover sheet should indicate if the initial sputum smears and cultures were positive and if drug susceptibility testing results are available.
Class B1 TB, Extrapulmonary	Applicants with evidence of extrapulmonary tuberculosis. Document the anatomic site of infection.
Class B2 TB, LTBI Evaluation	Applicants who have a tuberculin skin test ≥10 mm but otherwise have a negative evaluation for tuberculosis. The size of the TST reaction, the applicant's status with respect to LTBI treatment, and the medication(s) used should be documented. For applicants who had more than one TST, whether the applicant converted the TST should be documented (i.e., initial TST <10 mm but subsequent TST ≥10 mm).
Class B3 TB, Contact Evaluation	Applicants who are a recent contact of a known tuberculosis case. The size of the applicant's TST reaction should be documented. Information about the source case, name, alien number, relationship to contact, and type of tuberculosis should also be documented.

Source: Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ). "CDC Immigration Requirements: Technical Instructions for Tuberculosis Screening and Treatment, 2007." Available at http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html

Significant changes in the 2007 Technical Instructions for Tuberculosis Screening include requiring:

- Tuberculin skin tests (TST) for applicants <15 years of age in countries with a World Health Organization (WHO)-estimated tuberculosis incidence rate >20 per 100,000.
- A chest radiograph for all applicants <15 years of age with TST ≥5 mm. Mycobacterial cultures for applicants with chest radiographs suggestive of tuberculosis disease.
- Treatment under a directly observed therapy (DOT) program.
- Completion of treatment prior to immigrating to the United States, according to American Thoracic Society/CDC/Infectious Diseases Society of America guidelines.
- New TB classifications for all applicants with suspected latent *Mycobacterium tuberculosis* infection and for contacts for cases of tuberculosis disease.

A detailed comparison on the 1991 and 2007 Technical Instructions is available at http://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/tuberculosis-guidelines.html#table1

The guideline for diagnosis of LTBI is still a TST of greater than or equal to 10 mm of induration. However, the trigger for a chest radiograph for persons being evaluated under the 2007 technical instructions is 5 mm of induration.

Policy

Newly arrived immigrants, refugees and asylees with Class B1/B2/B3 TB will receive thorough and timely TB evaluations and appropriate treatment to ensure prompt detection of TB disease and prevention of future cases.

Follow-up of B1, B2, and B3 Tuberculosis Arrivals

Division of Global Migration and Quarantine Forms

The Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ) generates the following Class B notification forms:

- **Follow-up Worksheet**
- DS-2053: “Medical Examination for Immigrant or Refugee Application”
- DS-3024: “Chest Radiograph and Classification Worksheet”

The DGMQ sends the notifications to Washington State Department of Health Tuberculosis Services. The DGMQ also sends a letter to any immigrant, refugee or asylee with a tuberculosis (TB) condition, indicating that a follow-up is needed in the United States.

The Washington State Department of Health Tuberculosis Services notifies local health jurisdictions of arrivals by forwarding the B1/B2/B3 notifications to the county designated as the intended residence of the immigrant, refugee or asylee.

Electronic Disease Notification Process Overview

EDN Process Flowchart

The Washington State Department of Health receives notification of newly arrived immigrants, refugees and asylees electronically from the Centers for Disease Control and Prevention through the Electronic Disease Notification (EDN) system. Records from overseas medical examinations are downloaded and sent to local health jurisdictions or their designated local screening agencies.

The local health jurisdiction completes the evaluation of the new arrival and returns a completed Follow-Up Worksheet to the Department of Health via fax or mail. Follow-up worksheets should be submitted to DOH (1) No later than 90 days from arrival date into the United States and (2) When therapy for active disease or latent tuberculosis infection is completed.

If the local health jurisdiction is unable to locate the new arrival, the new arrival has moved, or they fail to come to scheduled appointments; the paperwork is returned to the Department of Health with an explanation as to why the evaluation was unable to be completed.

At the Department of Health a designated staff member enters data from returned Follow-up Worksheets into the Electronic Disease Notification database and submits it to the Centers for Disease Control and Prevention. This data assists in tracking the progress of National/State Objectives & Measures.

Notes:

1. When contacting the Department of Health about the status of a new arrival where paperwork has not been received yet from the Electronic Disease Notification system, please use the person's alien number and date of entry into the United States in all correspondence. This information is needed to track individuals within the system.

Patient Follow-up

The immigration paperwork may make it appear that a patient has had a complete evaluation for TB disease. However, under the 1991 guidelines, the overseas evaluation is designed only to detect abnormal radiographs and to determine *infectiousness* at the time of travel. The evaluation does not rule out TB disease. Under the 2007 guidelines, a more thorough evaluation is done overseas. However, individuals may enter the United States with “non-infectious” tuberculosis disease, such as extrapulmonary tuberculosis. All B1 and B2 arrivals under the 1991 guidelines need a new diagnostic evaluation for active disease, including a tuberculin skin test or IGRA test, a new chest radiograph and sputum cultures if symptomatic or chest radiograph indicative of tuberculosis. Even if active TB disease is ruled out, most B1 and B2 arrivals are priority candidates for treatment of latent TB infection (LTBI). Under the 2007 guidelines, B1 arrival evaluation is the same (except AFB cultures as well as smears are obtained) B2 arrivals need to be evaluated for LTBI as do B3 arrivals who are contacts to cases in their country of origin.

Suggested follow-up of each B1, B2 or B3 arrival is described below. (The term “Immigrant” used in the rest of this document includes all three categories: immigrants, refugees and asylees)

1. Determine if the immigrant has already visited the health department.
2. If not, make a telephone call to the home of the immigrant’s sponsor or relative after receiving the notification. Arrange for the immigrant to come in during clinic hours at the health department and/or arrange for the patient to see a private provider.
3. If the immigrant does not visit the health department or a private provider after the telephone call, send a letter to the home of the immigrant’s sponsor or relative.
4. If the immigrant does not visit the health department or a private provider after receiving the letter, visit the home of the immigrant’s sponsor or relative. If indicated, bring with you a representative who speaks the immigrant’s first language, if at all possible.
5. Every effort should be made to locate B1, B2 and B3 arrivals as these immigrants are considered high risk for TB disease.
6. Complete the Class B follow-up.
7. Complete and return the B notification Follow-up form to Washington State TB Services. This form is essential for Washington State TB Services to conduct statewide surveillance and follow-up on all B1, B2 and B3 arrivals and report the results to the CDC.

For more information on screenings, the Spokane Regional Health District provides an example of a Refugee Program Manual.

Evaluation of B1 and B2 Tuberculosis Arrivals

Evaluation Activities

Upon receipt of immigration paperwork, the local health jurisdiction needs to look at what country the immigrant comes from to determine whether they have been screened according to the 1991 or 2007 Technical Instructions. If unsure whether the country of origin is under the new Technical Instructions, go to http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-implememtation.html for a current list.

Arrivals from countries still under the 1991 Guidelines:

B1 arrivals had overseas sputum samples that were negative for acid-fast bacilli on smear and overseas chest radiographs that are abnormal and suggestive of **active TB disease**

B2 arrivals had overseas sputum samples that were negative for acid-fast bacilli on smear and overseas chest radiographs that are abnormal and suggestive of **inactive TB disease**.

Refer to Tables 6 and 7 to determine which evaluation tasks should be done for B1, B2 and B3 arrivals.

Table 5: Evaluation Activities for B1 and B2 Arrivals 1991 Guidelines

Evaluation Activities	B1 Active TB	B2 Inactive TB
• Determine tuberculin skin test (TST) status. If documentation is not available, administer a TST. A reaction of ≥5 mm is considered significant for persons with an abnormal chest radiographs. • Screening may also be done using the IGRA blood test.	Yes	Yes
• Review the chest radiograph.. Even if patients have their overseas chest radiographs available, a new chest radiograph must be taken.	Yes	Yes
• Review TB treatment history with the patient. Treatment history may be on the visa medical examination report form DS-2053: *Medical Examination for Immigrant or Refugee Application.* In some cases, patients have received treatment not documented on the DS-2053. • Regardless of the chest radiograph result, collect sputum specimens if the patient is symptomatic.	Yes	Yes
• Collect sputum for testing. Sputum specimens should be collected 8 to 24 hours apart, with at least one being an early morning specimen. • Regardless of the chest radiograph result, collect sputum specimens if the patient is symptomatic.	Yes	If symptoms present

Sources: Curry International Tuberculosis Center. Recommended TB clinic procedures for Class B1 TB arrivals and recommended TB clinic procedures for Class B2 TB arrivals. In: Text: step-by-step guide. *B Notification Assessment and Follow-up Toolbox* [Curry International Tuberculosis Center Web site]. San Francisco, CA; January 2004.

TABLE 6: EVALUATION ACTIVITIES FOR B1, B2 AND B3 ARRIVALS UNDER 2007 GUIDELINES[6]

Evaluation Activities	B1 Active/Inactive TB	B2 LTBI	B3 Contacts
• **Determine tuberculin skin test (TST) status.** If documentation is not available, administer a TST. A reaction of ≥5 mm is considered significant for persons with an abnormal chest radiograph.	Yes	Yes	Yes
• **Review the chest radiograph.** Even if patients have their overseas chest radiographs available, a new chest radiograph must be taken.	Yes	Yes, if TST positive	Yes, if TST positive
• **Review TB treatment history with the patient.** Treatment history may be on the visa medical examination report, form DS-2053: *Medical Examination for Immigrant or Refugee Application.* In some cases, patients have received treatment not documented on the DS-2053.	Yes	Yes	Yes
• **Collect sputum for testing.** Sputum specimens should be collected 8 to 24 hours apart, with at least one being an early morning specimen.	Yes	If symptoms present	If symptoms present

Sources: Curry International Tuberculosis Center. Recommended TB clinic procedures for Class B1 TB arrivals and recommended TB clinic procedures for Class B2 TB arrivals. In: Text: step-by-step guide. *B Notification Assessment and Follow-up Toolbox* [Curry International Tuberculosis Center Web site]. San Francisco, CA; January 2004.

Documentation

The Follow-up Worksheet will be sent to the local health jurisdiction with the overseas medical evaluation information for each immigrant. It will be filled in manually by the medical provider, then entered into the Electronic Disease Notification (EDN) system by DOH staff.

The following form assists in completing the Follow-up Form:

DOH Instructions for completing Follow-up Form

Forms also available in the **FORMS** section of the manual.

Treatment

Prescribe medications as appropriate. ***Do not start patients on single-drug therapy for latent TB infection (LTBI) until tuberculosis (TB) disease is ruled out.*** B1/B2/B3 immigrants with positive tuberculin skin tests or IGRA tests for whom active TB has been ruled out are priority candidates for treatment of LTBI because of the increased probability of recent infection and subsequent progression to active TB disease. Patients with fibrotic lesions on a chest radiograph suggestive of old, healed TB are candidates for treatment of LTBI, regardless of age.

The overseas diagnosis of clinically active TB disease under the 1991 guidelines is based upon the abnormal chest radiograph. Reevaluation in the United States may show the patient to actually have old, healed TB. According to current CDC/American Thoracic Society (ATS) recommendations, old, healed TB can be treated with four months of isoniazid and rifampin or with nine months of isoniazid.[2]

For more information on treatment, see the Centers for Disease Control and Prevention *Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection* (MMWR June 9, 2000/vol 49/RR-6) at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

Resources and References

Resources

- California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). "Guidelines for the Follow-up and Assessment of Persons with Class B1/B2 Tuberculosis" *(CDHS/CTCA Joint Guidelines;* September 1999). Available at: http://www.ctca.org/fileLibrary_54.pdf .
- Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ). "Medical Examinations of Aliens (Refugees and Immigrants)" (CDC Web site; accessed September 25, 2006). Available at: http://www.cdc.gov/ncidod/dq/health.htm .
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- Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ). Comparison of 2007 Technical Instructions for Tuberculosis Screening and Treatment with 1991 Instructions. Available at http://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/tuberculosis-guidelines.html#table1
- Curry International Tuberculosis Center. *B-Notification Assessment and Follow-up Toolbox* (Curry International Tuberculosis Center Web site; January 2004).

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[1] California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). Guidelines for the follow-up and assessment of persons with Class B1/B2 tuberculosis. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. September 1999:1. Available at: http://www.ctca.org/fileLibrary_54.pdf .
Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):2.

[2] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):34.

[3] CDC. Immigrant and Refugee Health. About Refugees. Available at http://www.cdc.gov/immigrantrefugeehealth/about-refugees.html.

[4] Martin, C. and Hoefer, M. Homeland Security: Office of Immigration Statistics. Annual Flow Report: Refugees and Asylees: 2010. (May 2011). Available at http://www.dhs.gov/xlibrary/assets/statistics/publications/ois_rfa_fr_2010.pdf

[5] CDC. CDC Immigration Requirements: Technical Instructions for Tuberculosis Screening and Treatment 2007. Available at http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html

DOH 343-071 June 2012
For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

Diagnosis of Tuberculosis Disease

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Forms Used in this Section

- Acknowledgement of TB Counseling (PHSKC)
- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Chart Audit Tool
- Civil Detention Flowchart
- Clinic Record (SHD)
- Contact Investigation
- Contact Investigation Instructions
- Do Not Board (DNB) Protocol
- Home Evaluation (SHD)
- Home Isolation Agreement (SHD)
- Isolation Instructions (TPCHD)
- Isolation Instructions/Spanish (TPCHD)
- QFT: TB Control Guidelines for Public Health Staff (Thurston County)
- RVCT Form (CDC)
- Protocol and Standing Orders (SHD)
- Public Health Directive (Adherence) (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)
- Screening Record (SHD)
- Tuberculosis Screening Guidelines
- Voluntary Isolation/Quarantine Agreement (TPCHD)

Quick Start Check List: Diagnosis of Tuberculosis Disease

This check list is designed to assist public health nurses when evaluating a patient for tuberculosis disease. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Tuberculosis Disease	Instructions and Forms
Start the initial assessment of the patient within ≤1 business day of the case report	**Instructions:** Effective TB Interviewing for Contact Investigation • http://www.cdc.gov/tb/publications/guidestoolkits/Interviewing/default.htm **Forms:** • Home Evaluation (SHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart • Chart Audit Tool
Take infection control precautions: ☐ Isolate the patient, if necessary (if the patient has positive acid-fast bacilli [AFB] sputum smear results and/or cavitary disease) ☐ Advise staff to take personal respiratory precautions, if necessary	**Instructions:** • Infection Control (**11.1**) **Forms:** • Letter of Isolation (SHD) • Isolation Instructions (TPCHD) • Isolation Instructions-Spanish (TPCHD) • Voluntary Isolation/Quarantine Agreement (TPCHD)
Evaluate the patient: ☐ Initiate immediate medical evaluation of patient, if not already done ☐ Assure that a medical evaluation of the patient is completed within 1 week of referral ☐ Gather medical history ☐ Screen for human immunodeficiency virus (HIV)	**Instructions:** • Protocol and Standing Orders (SHD) • Tuberculosis Screening Guidelines **Forms:** • Clinic Record (SHD) • Screening Record (SHD) • Acknowledgement of TB Counseling (PHSKC)

Tasks for Diagnosis of Tuberculosis Disease	Instructions and Forms
Evaluate the patient (continued): ☐ Conduct a physical examination ☐ Administer, measure, and interpret a Mantoux tuberculin skin test or a IGRA ☐ Order chest radiography ☐ Collect and submit 3 sputum specimens for AFB smear and culture. Obtain specimens 8 to 24 hours apart with one being an early morning specimen ☐ Receive, review and document results of AFB sputum smear tests ☐ Assure that a nucleic acid amplification (NAAT) test is ordered to quickly identify MTB Complex for a patient highly suspicious to have pulmonary tuberculosis. ☐ Reassess information about the patient weekly until drug susceptibility results are available and then at least monthly thereafter ☐ Assess patient for need to restrict travel (do not board)	• Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart **Instructions:** • Laboratory Testing (**10.1**) • In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101 Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx • Do Not Board Protocol
Monitor laboratory test results for culture and drug susceptibility: ☐ Receive, review and document culture results ☐ Receive, review and document drug susceptibility results as soon as available, usually about four weeks after the patient's initial specimen collection date	**Instructions:** • Available Laboratory Tests (Lab Section) (**10.8**) • The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Persons being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm **Forms:** • Clinic Record (SHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart

Tasks for Follow up of Patients Diagnosed with Tuberculosis Disease	Instructions and Forms
Communicate to Washington State TB program staff: ☐ Enter information into PHIMS TB within 7 days of the LHJ receiving notification of the suspect OR case ☐ Submit the Contact Investigation form to WA State TB Services within 2 weeks	**Forms:** • Contact Investigation • Instructions
Start the patient on treatment for TB disease	**Instructions:** • Treatment of Disease (**5.1**)
Manage the case	**Instructions:** • Case Management (**8.19**)
Conduct the contact investigation ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Forms:** • Contact Investigation • Instructions

The following "Tuberculosis Screening Guidelines" can be used to understand the evaluation process in diagnosing TB disease and LTBI.

TUBERCULOSIS SCREENING GUIDELINES

Washington State Clinical Laboratory Advisory Council

GROUP 1 - HIGHEST PRIORITY. Close contacts (i.e. sharing same household or other enclosed environments) of persons who have suspected or confirmed TB. Patients with or at risk of HIV infection

Screening persons other than members of high risk groups is NOT recommended

CXR= Chest X-Ray
LTBI = Latent TB infection
MOTT = Mycobacteria Other Than TB
QFT-G = QuantiFERON - TB Gold
TST = Mantoux 5TU TST
(See reverse side for interpretation of skin test results)

GROUP 2 - HIGH RISK GROUPS. Persons who inject illicit drugs. Persons with medical risk factors (i.e. diabetes mellitus; prolonged use of corticosteroids and other immunosuppressive therapy; chronic renal failure; leukemias/lymphomas; carcinoma of head/neck; weight loss of > 10% of ideal body weight; silicosis; gastrectomy; jejunoileal bypass). Residents/employees of high risk congregate setting (i.e. correctional institutions; nursing homes; homeless shelters; drug & alcohol treatment centers; healthcare facilities). Persons recently arrived from countries having high prevalence of TB. Medically underserved, low-income populations. Locally identified high-risk groups. Children and adolescents exposed to adults in high-risk categories.

TST AND CXR

TST (+/-) CXR Abnormal

TST (-) CXR Normal

TST (+) CXR Normal

If close contact, retest with TST in 8-10 weeks;initiate treatment for LTBI for close contacts who are immunocompromised or <5 years old.

3 month TST (-)** (Consider Stopping Treatment)

3 month TST (+)

Refer for clinical evaluation and LTBI treatment

TST (see reverse side for information and use of QuantiFERON)

Positive

Negative

CXR

Normal

Abnormal

No Further Action unless suspected anergy or clinical illness*

***Sputum Culture: 3 consecutive sputum specimens can be collected 8-24 hours apart with one being in the early morning.

Perform fluorochrome smear on concentrated specimens.

Inoculate rapid isolation (radiometric / non-radiometric system) AND solid medium.

Smear (+) Perform AMTD**** on all 1st time positive smears

Culture (-)

Culture (+)

Smear (-) Perform AMTD**** upon request if clinically suspected or as part of an outbreak investigation

Culture (-)

Evaluate for empiric treatment, if clinically indicated

Perform Rapid ID (DNA Probe, Biochemicals)

TB

MOTT

Perform BACTEC or Plate Susceptibility Test

Species identification by: DNA Probes, HPLC, GLC or biochemical tests

Evaluate for Treatment

For patients with positive AFB smears at the time of diagnosis, collect sputums every 2 weeks until 2 consecutive specimens are smear negative

Collect sputums at monthly intervals until 2 consecutive specimens are culture negative. **NOTE:** If culture positive after 3 months, consider resistance, non-compliance, or non-absorption.

* See reverse side for discussion on TST

** Consider stopping treatment if the TST is negative at 3 months. If there should be continued exposure to an infectious case during that time, the more susceptible person may need to stay on medication longer.

*** Other specimens may be submitted for TB testing, e.g. bronchoscopically acquired specimens, pleural fluid, biopsies, etc.

**** AMTD (Amplified *M. tuberculosis* Direct Test) A rapid molecular diagnostic test performed on raw respiratory specimens. Use the first time the patient has a positive smear or if requested to test on negative smears when patient is suspected of having TB.

FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient.

Originally published: April 1997
Reviewed/Revised: Oct 2000/Oct 2003/ May 2004/April 2007

INTERPRETATION OF TUBERCULIN SKIN-TEST (TST) RESULTS

A. ≥5mm is positive for: . Recent close contacts of persons with active TB . Persons with HIV infection . Persons with fibrotic CXR consistent with healed TB . Organ transplant recipients and other immunosuppressed patients	**B. ≥10mm is positive** for persons who do not meet the criteria in (A.) and who belong to one or more of the following: . Injection-drug users . Persons with other medical conditions reported to increase risk of progressing from latent to active TB (see list in Group 2 box on the reverse side) . Residents/employees of high-risk congregate settings (i.e. correctional institutions, nursing homes, homeless shelters, drug & alcohol treatment centers, healthcare facilities) . Persons recently arrived from countries having high prevalence of TB (e.g. ≤ 5 years since arrival) . Medically underserved, low-income populations . Locally identified high-risk groups . Children of any age exposed to adults in high-risk categories	**C. ≥15mm is positive** for persons with no risk factors for TB
ANERGY . Anergy testing is poorly standardized or can be selective (e.g. anergy or reactivity to mumps or candida may not reliably predict anergy or ability to respond to TST). . Should not be routinely used as part of screening for TB even in HIV infected patients.	**BOOSTER EFFECT** . Persons with TB infection may have negative TST when tested many years after infection . Initial TST may stimulate (boost) ability to react to PPD . Positive reactions to subsequent tests may be misinterpreted as new infection . See Two-Step Testing	**TWO-STEP TESTING** For baseline skin testing of adults who will be retested periodically to distinguish boosted reactions from reactions due to new infections: . If first test is (+), consider person infected at baseline . If first test (-), give second test 1-3 weeks later . If second test (+), consider person infected at baseline . If second test (-), consider person uninfected at baseline

QuantiFERON (QFT): The Centers for Disease Control and Prevention (CDC) Guidelines for the use of QFT in diagnosing Latent *Mycobacterium tuberculosis* Infection (LTBI) can be found in the Morbidity Mortality Weekly Report (MMWR), January 31, 2003, Volume 52, pages 15-18 (http://www.cdc.gov/mmwr/PDF/rr/rr5202.pdf). CDC states that QFT can aid in detecting *M. tuberculosis* infections among certain populations who are at increased risk for LTBI including recent immigrants from countries with a high prevalence of TB infection, injection-drug users, residents and employees of prisons and jails, and healthcare workers that, after their pre-employment assessment, are considered at increased risk for exposure to TB. CDC states that QFT may also be used for military personnel screening, hospital staff and health-care workers whose risk of prior exposure to TB was low, and U.S.-born students at certain colleges and universities. The full text of the CDC document can be found at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a2.htm.

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1. Centers for Disease Control and Prevention. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49:RR-6.
2. American Thoracic Society/CDC. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med 2000; 161:1376-1395.
3. CDC. Core Curriculum on Tuberculosis. Fourth Edition. DHHS, 2000.
4. ATS/CDC. Treatment of Tuberculosis and Tuberculosis Infection in Adults and Children. Am J Resp Crit Care Med 1994;149:1359-1374.
5. CDC. Guidelines for Using the QuantiFERON-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection USA. MMWR, Dec. 16, 2006, Vol. 54 (RR15), pages 49-55.
6. American Thoracic Society/CDC/Infectious Diseases Society of America: Treatment of Tuberculosis. 2003. Respir Crit Care Med, vol.167, pp 603-662.

Introduction

Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Classify patients with tuberculosis (TB) disease and latent TB infection (LTBI).
- Detect suspected cases of TB.
- Know when to report suspected or confirmed cases of TB.
- Diagnose TB disease.

It is important to understand when a person should be evaluated further for TB disease. Not recognizing TB symptoms promptly will lead to delays in treating a TB case—and to more infection, TB disease, and contacts to evaluate.

In the 2005 guideline, "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment.[1]

Contacts are mentioned within this section, but their evaluation and follow-up and contact investigation are covered in more depth in the Contact Investigation section of the manual (**9.1**)

Improvement in the detection of TB cases is essential to progress toward elimination of TB in the United States.[2] Case detection includes the processes that lead to the presentation, evaluation, receipt of diagnosis, and reporting of persons with active TB.[3] Detecting and reporting suspected cases of TB are key steps in stopping transmission of *Mycobacterium tuberculosis* because it leads to prompt initiation of effective multiple-drug treatment, which rapidly reduces infectiousness.[4]

TB is commonly diagnosed when a person seeks medical attention for symptoms caused by the disease or a concomitant medical condition. Thus, healthcare providers, particularly those providing primary healthcare to populations at high risk, are key contributors to TB case detection.[5] The majority of pulmonary TB cases continue to be diagnosed at an advanced stage. Earlier diagnosis would result in less individual morbidity and death, greater success in treatment, less transmission to contacts, and fewer outbreaks of TB.[6]

A diagnosis of TB disease is usually based on positive cultures for *M. tuberculosis.* However, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture.

Policy

In Washington State:

- Persons who show or report signs and symptoms of TB should be evaluated for TB disease as described in the "Diagnosis of Tuberculosis Disease" topic in this section of the manual (**4.1**) and reported as suspected cases of TB as described in the "Reporting Tuberculosis" topic in the Surveillance section of the manual (**2.8**).
- Contacts should be evaluated as described in the Contact Investigation section of the manual (**9.1**)

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction of the manual (**1.16**).

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

To identify required and recommended forms, refer to the "Quick Start Check List: Diagnosis of Tuberculosis Disease" in this section of the manual or check the **FORMS** section of the manual.

Case Finding

Identifying Suspected Tuberculosis Cases

The majority of tuberculosis (TB) cases are detected during the medical evaluation of symptomatic illnesses. Persons experiencing symptoms ultimately attributable to TB usually seek care not at a public health TB clinic but rather from other medical practitioners in other healthcare settings.[7] Professionals in the primary healthcare sector, including hospital and emergency department clinicians, should be trained to recognize patients with symptoms consistent with TB.[8]

Be alert for cases of TB among persons who have not sought medical care during evaluation of contacts to patients with pulmonary TB and to other persons with newly diagnosed infection with *Mycobacterium tuberculosis.* Perform screening for TB also during evaluation of immigrants and refugees with Class B1 or Class B2 TB notification status, during evaluations of persons involved in TB outbreaks, and occasionally in working with populations with a known high incidence of TB. Also, screen for TB disease when the risk for TB in the population is high and when the consequences of an undiagnosed case of TB are severe, such as in jails, prisons, and other correctional facilities.[9]

Suspect pulmonary TB and initiate a diagnostic investigation when the historic features, signs, symptoms, and radiographic findings listed in Table 1 occur among adults. The clinical presentation of TB varies considerably as a result of the extent of the disease and the patient's response. **TB should be suspected in any patient who has a persistent cough for more than 2 to 3 weeks, or other compatible signs and symptoms**.[10]

Note that these symptoms should suggest a diagnosis of TB but are not required. TB should still be considered a diagnosis in asymptomatic patients who have risk factors for TB and chest radiographs compatible with TB.

All persons who have a chronic cough for more than 2 to 3 weeks[11] should be evaluated and be asked to use a mask or tissue to cover their mouth. Hemoptysis, or coughing up blood, is a serious symptom, and patients who cough up blood should be evaluated as soon as possible. Be sure to have these patients use a mask and tissues.

TABLE 1: WHEN TO SUSPECT PULMONARY TUBERCULOSIS IN ADULTS[12]

Historic Features	• Exposure to a person with infectious tuberculosis (TB) • Positive test result for *Mycobacterium tuberculosis* infection • Presence of risk factors, such as immigration from a high-prevalence area, human immunodeficiency virus (HIV) infection, homelessness, or previous incarceration • Diagnosis of community-acquired pneumonia that has not improved after 7 days of treatment[†,13]
Signs and Symptoms Typical of TB	• Prolonged coughing (≥2–3 weeks) with or without production of sputum that might be bloody (hemoptysis)[§,14] • Chest pain[15] • Chills[16] • Fever • Night sweats • Loss of appetite[17] • Weight loss • Weakness or easy fatigability[18] • Malaise (a feeling of general discomfort or illness)[19]
Chest Radiograph: Immunocompetent patients	• Classic findings of TB are upper-lobe opacities, frequently with evidence of contraction fibrosis and cavitation[¶]
Chest Radiograph: Patients with advanced HIV infection	• Lower-lobe and multilobar opacities, hilar adenopathy, or interstitial opacities might indicate TB

† Patients treated with levofloxacin or moxifloxacin may have a clinical response when TB is the cause of the pneumonia.

§ Do **not** wait until sputum is bloody to consider a productive cough a symptom of TB. Sputum produced by coughing does **not** need to be bloody to be a symptom of TB.

¶ These features are not specific for TB, and, for every person in whom pulmonary TB is diagnosed, an estimated 10–100 persons are suspected on the basis of clinical criteria and must be evaluated.

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

Extrapulmonary Tuberculosis

If a patient has a positive tuberculin skin test or interferon gamma release assay (IGRA), consider signs and symptoms of extrapulmonary TB. See Available Laboratory Tests, Table 2 (**10.8**) for labs within Washington State that perform IGRA testing.

Follow-up on Suspected Cases of Tuberculosis

When a suspected case of TB is identified, the following should be done:

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

When a suspected case of pulmonary TB is identified, refer to Table 2: Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios in the "Diagnosis of Tuberculosis Disease" topic in this section. This table presents guidelines for the initial steps of TB case detection in five clinical scenarios encountered by providers of primary health care, including those serving in medical emergency departments.[20]

To formally report a suspected case of TB, see the "Reporting Tuberculosis" topic in the Surveillance section of the manual (**2.8**).

The patient should be masked and immediately excluded from the workplace or placed in airborne infection isolation (AII) until confirmed noninfectious. For more information, see the "Isolation" topic in the Infection Control section of the manual (**11.15**).

Laboratories must report positive smears and positives cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the local health jurisdiction, as specified in the "Reporting Tuberculosis" topic in the Surveillance section of the manual (**2.8**). Prompt reporting allows the local health jurisdiction to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[21]

Within 48 hours of suspect identification, administer a tuberculin skin test (TST) or perform an interferon gamma release assay (IGRA) and/or provide a chest radiograph (if these activities had not already been completed). Evaluate the patient for TB disease as specified in the "Diagnosis of Tuberculosis Disease" topic in this section of the manual (**4.1**).

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see the "Protocol and Standing Orders" form in the **FORMS** section of the manual.

Diagnosis of Tuberculosis Disease

Consideration of tuberculosis (TB) disease as a possible diagnosis is the first step that must be taken before further evaluation, diagnosis, and management can occur. The diagnosis of TB disease is often overlooked because of the failure to consider it among possible diagnoses. While a definitive diagnosis may involve the addition of laboratory and radiographic findings, a high degree of suspicion can be based on epidemiology, medical history, and physical examination. In considering TB disease, it is also important to consider factors that may affect the typical presentation of TB, such as the patient's age, nutritional status, and coexisting diseases.

An individual who is suspected of having TB disease requires a complete medical evaluation, including the following:

- Medical history, including exposure, symptoms, previous treatment for TB, and risk factors
- Human immunodeficiency virus (HIV) screening
- Physical examination
- Tuberculin skin test (TST) or interferon gamma release assay (IGRA)
- Chest radiography
- Bacteriologic examination

When a suspected case of pulmonary TB is identified, refer to Table 2 for guidelines for the initial steps of TB case detection in five clinical scenarios encountered by providers of primary healthcare, including those serving in medical emergency departments.[22]

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

TABLE 2: GUIDELINES FOR THE EVALUATION OF PULMONARY TUBERCULOSIS IN ADULTS IN FIVE CLINICAL SCENARIOS[23]

Patient and Setting	Recommended Evaluation
Any patient with a cough of ≥2–3 weeks' duration	Chest radiograph: If suggestive of tuberculosis (TB)*, collect 3 sputum specimens for acid-fast bacilli (AFB) smear microscopy, culture, and nucleic acid amplification (NAA).
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms of ≥2–3 weeks' duration†	Chest radiograph: If suggestive of TB, collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient with human immunodeficiency virus (HIV) infection and unexplained cough or fever	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient at high risk for TB with a diagnosis of community-acquired pneumonia who has not improved after 7 days of treatment†	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient at high risk for TB with incidental findings on chest radiograph suggestive of TB even if symptoms are minimal or absent†§	Review of previous chest radiographs, if available, 3 sputum specimens for AFB smear microscopy, NAA (available at PHL), and culture

* Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.[24]

† See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease.

§ Chest radiograph performed for any reason, including targeted testing for latent TB infection and screening for TB disease.

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

Medical History

The clinician should interview patients to document their medical histories. A written record of a patient's medical history should include the following:

- Exposure to infectious TB
- Symptoms of TB disease (as listed in Table 1: When to Suspect Pulmonary Tuberculosis in Adults, Table 2: Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios, and Table 3: Symptoms of Tuberculosis Disease)
- Previous TB infection or disease
- Risk factors
- Recent medical encounters (e.g., going to the emergency department for pneumonia)
- Previous antibiotic therapy

1. Exposure to infectious TB:
Ask patients if they have spent time with someone with infectious TB.

Question patients about whether they know of any contact in the recent or distant past with persons diagnosed with pulmonary or laryngeal TB. It is important to note that patients often refer to latent TB infection (LTBI) as TB disease. Be aware that most persons become infected with *Mycobacterium tuberculosis* without knowing they were exposed. Clinicians should also consider demographic factors that may increase a patient's risk for exposure to TB disease and drug-resistant TB, such as country of origin, age, ethnic or racial group, occupation, and residence in congregate settings (such as a jail, homeless shelter, or refugee camp).

2. Symptoms of TB Disease:
Ask patients about their symptoms.

Although TB disease does not always produce symptoms, most patients with TB disease have one or more symptoms that led them to seek medical care. When symptoms are present, they usually have developed gradually and been present for weeks or even months. Occasionally, however, TB is discovered during a medical examination for an unrelated condition, such as ruling out a cancer diagnosis (e.g., through a chest radiograph given to patients before surgery).

The symptoms in Table 3 below may be caused by other diseases, but they should prompt the clinician to suspect TB disease. For historic features and chest radiograph results that should raise suspicion of pulmonary TB disease, refer to Table 1: When to Suspect Pulmonary Tuberculosis in Adults**.**

TABLE 3: SYMPTOMS OF TUBERCULOSIS DISEASE[25]

Pulmonary	General: Pulmonary and Extrapulmonary	Extrapulmonary
• Coughing • Coughing up sputum or blood • Pain in the chest when breathing or coughing	• Chills[26] • Fever • Night sweats • Loss of appetite[27] • Weight loss • Weakness or easy fatigability[28] • Malaise (a feeling of general discomfort or illness)[29]	• The symptoms depend on part of body affected by tuberculosis (TB) disease • TB of the spine may cause pain in the back. • TB of the kidney may cause blood in the urine. • Meningeal TB may cause headaches or psychiatric symptoms. • Lymphatic TB may cause swollen and tender lymph nodes, often at the base of the neck. • Pleural • Laryngeal

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

3. Previous Latent TB Infection or TB Disease:
Ask patients whether they have ever been diagnosed with or treated for TB infection or disease.

- **Patients who have had TB disease before** should be asked when they had the disease and how the disease was treated. Ask how many pills were taken per day (to determine what treatment regimen was used and whether they received injections). If the regimen prescribed was inadequate or if the patient did not follow the recommended treatment, TB may recur, and it may be resistant to one or more of the drugs used.
- **Patients known to have a positive skin test reaction or positive Interferon Gamma Release Assay (IGRA)** probably have TB infection. If they were infected within the past two years, they are at high risk for TB disease if certain immunosuppressive conditions exist or if immunosuppressive therapies are being taken. For persons previously skin tested, an increase in induration of 10 mm within a two-year period is classified as a conversion to positive or positive Interferon Gamma Release Assay (IGRA).

4. Risk Factors for Developing TB Disease:
Determine whether patients have any conditions or behaviors that are risk factors for developing TB disease.

Human Immunodeficiency Virus Screening

Voluntary counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. HIV counseling and testing has also been recommended for contacts of persons with TB.[30]

The Centers for Disease Control and Prevention (CDC) recommends the following:

- HIV screening for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
- Routine HIV testing for persons suspected of having TB disease and contacts to TB patients.
- Persons at high risk for HIV infection should be screened for HIV at least annually[31]

New HIV testing, counseling, and partner services rules offer flexibility to health care providers and local health jurisdictions. Please visit http://www.doh.wa.lcl/YouandYourFamily/IllnessandDisease/HIVAIDS/Prevention/InformationforProviders.aspx for more information.

Physical Examination

A physical examination is an essential part of the evaluation of any patient. It cannot be used to confirm or rule out TB, but it can provide valuable information about the patient's overall condition; other factors, such as human immunodeficiency virus (HIV) infection, which may affect how TB is manifested; and the presence of extrapulmonary TB.[32]

Tuberculin Skin Test and Interferon Gamma Release Assays (IGRA)

Use the Mantoux tuberculin skin test (TST) or an interferon gamma release assay (IGRA) to test for *M. tuberculosis* infection. Note that for patients with a previous documented positive TST reaction, a TST is not necessary. However, an IGRA can be done if there is suspicion that the TST result was a false positive. Additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.[33]

Blood assay for *Mycobacterium tuberculosis* (BAMT) is a general term referring to recently developed in vitro diagnostic tests that assess for the presence of infection with *M. tuberculosis*. This term includes, but is not limited to IGRAs. The IGRAs currently approved by the Food and Drug Administration (FDA) and available on the market are QuantiFERON®-TB Gold in-tube (QFT™), QuantiFERON®-TB test (QFT), QuantiFERON®-TB Gold test (QFT-G) and the T-SPOT®.*TB* test**,** which can be used in all circumstances in which the TST is used. IGRA usually can be used in place of the TST.[34] Other cytokine-based immunoassays are under development and may also become useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products, in combination with Centers for Disease Control and Prevention (CDC)-issued recommendations, may provide additional diagnostic alternatives.[35]

The advantages of IGRA, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory, the variability associated with skin test reading can be eliminated.[36] In addition, the IGRA test appears to be less affected by past bacille of Calmette-Guérin (BCG) vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.[37] However, the IGRA test has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. For IGRA tests, the blood must be incubated with the test antigens less than 12 hours after collection, while the lymphocytes are viable.[38] (Note: When newer IGRA tests are available, this time frame may differ.)

For both the TST and IGRA, additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.[39]

Persons with a positive TST result, regardless of signs and symptoms, should be evaluated for TB disease before LTBI is diagnosed. At a minimum, a chest radiograph should be examined for abnormalities consistent with TB disease.[40]

A negative TST does not rule out TB disease[41]—as many as 20% of patients with TB disease have a negative TST reaction.[42] A negative TST result should not be used alone to exclude *M.*

tuberculosis infection in persons with symptoms or signs suggestive of TB disease. Medical evaluation of such persons should include a history and physical examination, chest radiograph, bacteriologic studies, serology for human immunodeficiency virus (HIV), and, when indicated, other tests or studies.[43]

For more information on the Mantoux TST, see the Diagnosis of Latent Tuberculosis Infection section of the manual (**6.1**).

For more information on IGRAs and the QuantiFERON®-TB Gold (QFT-G) Test, see the CDC's "Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States" (*MMWR* 2005;54[No. RR-15]) at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf .

CDC released new Interferon Gamma Release Assays (IGRA) guidelines on June 25, 2010, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" *(MMWR* 2010; 59 [No. RR-5];1-25) at http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf.

CDC has also developed the Interferon-Gamma Release Assays (fact sheet) that will assist you in learning more about IGRAs.
http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm

For more information regarding QFT healthcare worker guidelines see QFT: TB Control Guidelines for Public Health Staff (Forms Section).

Find answers to common questions posed by healthcare professionals on the use of QFT at
http://www.cellestis.com/IRM/Company/ShowPage.aspx?CPID=1588&EID=60701344.

Chest Radiography

A posterior-anterior radiograph of the chest is the standard view used for the detection and description of chest abnormalities in adults. In some instances, other views (e.g., lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.

Children younger than 5 years of age should receive posterior-anterior and lateral radiographs.[44]

Certain abnormalities on chest radiographs are suggestive, but are not diagnostic, of TB. In pulmonary TB, radiographic abnormalities are often seen in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. However, lesions may appear anywhere in the lungs and may differ in size, shape, density, and presence or absence of cavitation, especially in HIV-infected and other immunosuppressed persons.

In HIV-infected persons, pulmonary TB may present atypically on the chest radiograph. For example, TB may cause opacities without cavities in any lung zone, or it may cause mediastinal or hilar lymphadenopathy with or without accompanying opacities and/or cavities. In HIV-infected persons, almost any abnormality on a chest radiograph may indicate TB. In fact, the radiograph of an HIV-infected person with TB disease may even appear entirely normal.[45]

For more information on chest radiography, see the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (2006) at http://www.currytbcenter.ucsf.edu/radiographic/

Bacteriologic Examination

Refer to Table 4 below to determine the types of specimens needed to assist in the diagnosis of TB.

TABLE 4: SPECIMENS FOR DIAGNOSING TUBERCULOSIS DISEASE

Suspected Diagnosis	Specimen Needed
Pulmonary or laryngeal tuberculosis (TB)	Sputum (phlegm from deep in the lungs) samples for smear and culture examination. If a diagnosis of pulmonary TB cannot be established from sputum smear, other procedures may be necessary, including nucleic acid amplification (NAA), bronchoscopy, and gastric aspiration in children.
Extrapulmonary TB	Depending on the anatomical site, other clinical specimens are necessary, such as: • Urine • Cerebrospinal fluid • Pleural fluid • Pus or other aspirated fluid • Biopsy specimens • Blood

Refer to Table 5 below for information on the bacteriologic tests used to diagnose TB.

TABLE 5: BACTERIOLOGIC TESTS USED IN DIAGNOSING TUBERCULOSIS DISEASE[46]

Test	Description	Laboratory Turnaround Times
Acid-Fast Bacilli (AFB) Smear	• Provides the physician with a preliminary confirmation of the diagnosis. It usually is the first bacteriologic evidence of the presence of mycobacteria in a clinical specimen. • If positive, gives a semiquantitative estimate of the number of bacilli being excreted (which is of vital clinical and epidemiologic importance in assessing the patient's infectiousness).	• Within 24 hours from receipt of specimen in the laboratory.[47]
Nucleic Acid Amplification (NAA) Assay[48]	• A test done on sputum specimens for the direct and rapid identification of the *Mycobacterium tuberculosis* complex. • Allows for the amplification of specific target sequences of nucleic acids that will be detected by a nucleic acid probe. • Does not replace the need for routine AFB smear and culture.[49]	• Within 2-3 working days from receipt of specimen in the laboratory .[50,51]
Culture	• Usually necessary for species identification of all clinical specimens suspected of containing mycobacteria. • Is required for drug susceptibility testing and genotyping.	• Mycobacterial growth detection: within 14 days from specimen collection • Identification of mycobacteria: within 21 days from specimen collection [52,53]
Drug Susceptibility Testing	• For first-line drugs: Is performed on initial isolates of all patients to identify an effective antituberculosis regimen. • For both first-line and second-line drugs: Is repeated on interim isolates when a patient remains culture-positive after 3 months of treatment.[54,55]	• First-line drugs: within 30 days from specimen collection. • Second-line drugs: within 4 weeks from date of request. [56,57]
Drug Resistance Screening by Sequencing (DRSS)	• Allows rapid confirmation of MDR TB through the identification of genetic mutations associated with RIF and INH resistance – MDR case. Also the DRSS examines the genetic loci that are associated with resistance to the most effective second-line drugs, fluroquinolones (FQ) and the injectables amakacin (AMK), kanamycin (KAN) and capreomycin (CAP) will be examined. [58]	• DRSS results are available within 3-4 business days from the receipt of specimen at the WA PHL laboratory. • DRSS is a presumptive test and needs to be confirmed by traditional susceptibility testing. WA PHL performs confirmation for the First line drugs (up to 14 days MTBC identification) and Second line drug (28 days from the receipt of the specimen [reference cultures] or MTBC identification).

Sources: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.

Laboratories must report positive smears or positive cultures within **2 business days**, and primary healthcare providers should report **immediately** suspected and confirmed cases of TB to the local health jurisdictions, as specified in the "Reporting Tuberculosis" topic in the Surveillance section (**2.8**). See WAC 246-101. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[59]

For information on reporting, see the "Reporting Tuberculosis" topic in the Surveillance section of the manual (**2.8**).

For information on process for collecting specimens see the "Specimen Collection" topic in the Laboratory section of the manual (**10.13**).

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

The Curry International Tuberculosis Center has developed a web presentation on "Practical Solutions for TB Infection Control: Infectiousness and Isolation" available at http://www.currytbcenter.ucsf.edu/tbicweb/

For laboratory (**10.8**) services available at the Washington State Public Health Laboratory, contact TB Laboratory Supervisor at 206-418-5474.

Resources and References

Resources

- ATS, CDC, IDSA. "Diagnostic Standards and Classification of Tuberculosis in Adults and Children" (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: http://www.cdc.gov/tb/publications/PDF/1376.pdf .
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[9] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):34.

[10] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

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[12] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33; CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: http://www.cdc.gov/tb/education/corecurr/index.htm; CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med.* 2000;161:1378; CDC. Module 3: diagnosis of tuberculosis infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.

[13] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

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DOH 343-071 June 2012
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Treatment of Tuberculosis Disease

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Forms Used in this Section

- Acknowledgement of TB Counseling (PHSKC)
- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Case Initial Assessment/Education (Clark/Skamania Counties)
- Chart Audit Tool
- Civil Detention Flowchart
- Clinic Record (SHD)
- Clinic Record (Virginia)
- Do Not Board (DNB) Protocol
- DOT Agreement (PHSKC)
- DOT Agreement (Virginia)
- DOT Log (Virginia)
- Drug Interview Sheet (SHD)
- Drug-O-Gram (TPCHD)
- Home Evaluation (SHD)
- Medication Information (Georgia)
- Medication Orders (SHD)
- RVCT Form (CDC)
- Protocol and Standing Orders (SHD)
- Public Health Directive (Adherence) (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)
- TB Control Referral (SHD)
- Treatment Agreement (TPCHD)
- Treatment Agreement (Spanish) (TPCHD)
- Tuberculosis Screening Guidelines
- Vision and Hearing Log (Virginia)

Quick Start Check List: Treatment of Tuberculosis Disease

This check list is designed to assist public health nurses when treating a patient for tuberculosis disease. Its high-level list of tasks provides an overview and to help staff know where to access important instructions and identify available forms. The tasks listed below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Tuberculosis Disease	Instructions and Forms
Perform the initial assessment of the patient	Forms: • Case Initial Assessment/Education (Clark/Skamania Counties)
Evaluate the patient	Instructions: • Treatment of Tuberculosis Disease (5.1) Forms: • Home Evaluation (SHD)
Follow basic principles for tuberculosis (TB) disease	Instructions: • Basic Treatment Principles (5.8) • Protocol and Standing Orders (SHD) • Chart Audit Tool
Plan and initiate treatment for TB disease: ☐ Initiate medical treatment as soon as possible after positive acid-fast bacilli (AFB) sputum smear results ☐ Obtain baseline biochemistry tests for toxicity monitoring (choose tests based on regimen and for special situations such as human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy): • Complete blood count • Platelets • Liver function tests ☐ Perform baseline visual acuity and color discrimination tests for toxicity monitoring if the patient is prescribed ethambutol	Instructions: • TB Screening Guidelines • Adverse Effects (5.19) Forms: • Clinic Record (SHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart

Tasks for Treatment of Tuberculosis Disease	Instructions and Forms
Plan and initiate treatment for TB disease (continued): ☐ Assess patient for need to restrict travel (do not board) ☐ Assure that an appropriate treatment regimen, dosages, and duration are selected. The preferred regimen for treating TB disease consists of an initial 2-month phase of 4 drugs: isoniazid, rifampin, pyrazinamide, and ethambutol followed by a 4-month continuation phase of isoniazid and rifampin[1] ☐ Assure that the following special situations are considered: • Drug-resistant TB • HIV infection • Alcoholism • Liver disease • Renal insufficiency and end-stage renal disease • TB associated with tumor necrosis factor-alpha antagonists • Culture-negative pulmonary TB • Extrapulmonary TB • Pregnancy and breastfeeding • TB in children ☐ Assure that a written treatment plan is developed ☐ Assure that the patient and provider are aware of and educated about the treatment plan ☐ Begin implementing the treatment plan	Forms: Instructions For Visual Acuity http://www.toledo-bend.com/colorblind/Ishihara.asp • Do Not Board Protocol • Treatment Agreement (TPCHD) • Treatment Agreement (Spanish) (TPCHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart • Tuberculosis Control Referral (SHD)
Monitor the patient regularly: ☐ Assess adherence and drug toxicity at each directly observed therapy (DOT)/Videophone (VDOT) ☐ Conduct ongoing assessment and monitoring at least monthly for clinical response, drug toxicity, and adherence ☐ Reassess treatment and, if concerned about response or drug toxicity, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs ☐ Receive and review drug susceptibility results 1 to 2 months after the patient's initial sputum collection date. ☐ Consult with WA State TB Services Medical Consultant at 206-718-2664 if drug susceptibility results show drug resistance to first-line drugs.	Instructions: • DOT/Videophone DOT (8.51) • Adverse Effects (5.19)

Tasks for Treatment of Tuberculosis Disease	Instructions and Forms
	• The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Persons Being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm Forms: • DOT Agreement (Virginia) • DOT Agreement (PHSKC) • Medication Orders (SHD) • Drug Interview Sheet (SHD)
Monitor the patient for drug toxicity: ☐ Assess drug toxicity at each DOT visit ☐ Repeat liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) when the patient is taking isoniazid, a rifamycin, or pyrazinamide if • Baseline results are abnormal • The patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • The patient has symptoms of adverse reactions ☐ If the patient is taking ethambutol, question the patient monthly regarding possible visual disturbances, including blurred vision or scotomata ☐ Test visual acuity and color discrimination monthly when the patient is taking ethambutol ☐ Assess patient for need to restrict travel (do not board)	Instructions: • Adverse Effects (5.19) Forms: • RVCT Form • Drug Interview Sheet (SHD) • Clinic Record (Virginia) • DOT Log (Virginia) • Vision and Hearing Log (Virginia) • Medication Information (Georgia) Instructions For Visual Acuity • http://www.toledo-bend.com/colorblind/Ishihara.asp • Do Not Board Protocol
Assess the patient's response to treatment: ☐ If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+ or greater (3+, 4+), then each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported ☐ When the patient has negative AFB sputum smear results, then each month collect sputum specimens and submit them for testing until 2 consecutive negative culture results are reported • For multidrug-resistant TB (MDR-TB) patients, monthly sputum specimens are required • For non-MDR-TB patients who can produce sputum, monthly specimens are recommended	Instructions: • Response To Treatment (5.29) Forms: • RVCT Form
Tasks for Treatment of Tuberculosis Disease	Instructions and Forms

Assess the patient's response to treatment (cont): ☐ If sputum smear results are positive after 2 months of treatment discuss with Medical Care Provider, Local Health Officer or WA State TB MD Consultant. ☐ Take the following actions if cultures or smears remain positive and symptoms continue after 3 months of treatment: ▪ Evaluate the patient for drug-resistant TB ▪ Provide DOT if the patient is self-administering medication ▪ Consult with Medical Care Provider, Local Health Officer or WA State TB Services Medical Consultant	
Confirm the completion of treatment: ☐ Verify completion of treatment 6 to 9 months after treatment was started depending upon • Regimen • Adherence • Response to treatment • Number of weeks on DOT • Number of doses taken	Forms: • RVCT Form

Introduction

Purpose

The overall goals for treatment of tuberculosis (TB) are to cure the patient and to minimize the transmission of *Mycobacterium tuberculosis* to others. Successful treatment of TB has benefits both for the individual patient and the community in which the patient resides.

Use this section to understand and follow national and Washington State guidelines to do the following:

- Follow basic treatment principles for TB disease
- Select appropriate treatment regimens, dosages, and duration
- Monitor patients for side effects and adverse reactions
- Assess patients' response to treatment
- Determine completion of therapy
- Determine the need for post-treatment evaluation
- Provide treatment in special situations, such as when a patient has drug-resistant TB or TB–human immunodeficiency virus (HIV) coinfection
- Hospitalize and coordinate hospital discharges of patients with infectious TB

In the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment.[2]

Forms

To identify required and recommended forms, refer to the "Quick Start Check List: Treatment of Tuberculosis Disease" in this section of the manual (**5.3**), or go to the **FORMS** section.

Basic Treatment Principles

Follow the basic treatment principles for tuberculosis (TB) disease, as outlined below in Table 1.

TABLE 1: BASIC TREATMENT PRINCIPLES FOR TUBERCULOSIS DISEASE

Phase	Principles
At Start of Treatment	Patient-centered care and directly observed therapy (DOT)/Videophone DOT. An adherence plan should tailor treatment and supervision to each patient by considering his or her clinical and social circumstances (patient-centered care), as well as emphasizing DOT/Videophone DOT.
	Cultural competence. It is imperative to become culturally competent and guide other healthcare providers toward culturally competent healthcare. A culturally competent system acknowledges cultural differences regarding healthcare and incorporates them into all levels of the healthcare delivery system, from policy to provider to patient.
	Human immunodeficiency virus (HIV) testing. HIV testing should be offered to all patients with TB disease.
	Medical supervision. Patients with confirmed or suspected tuberculosis (TB) disease must be under the medical supervision of a provider who is licensed in the State of Washington as a medical physician.
	Prompt start. Start patients with confirmed or suspected TB disease promptly on appropriate treatment. It is not necessary to wait for laboratory confirmation.
Regimen During Treatment	Multiple drugs. Treatment regimens must contain multiple drugs to which the organism is susceptible. The administration of a single drug or the addition of a single drug to a failing regimen can lead to the development of resistance.
	Single doses. TB medications should be administered together as a single dose rather than in divided doses. A single dose leads to higher and potentially more effective, peak serum concentrations, and facilitates DOT. Although ingesting the medications with food will delay or moderately decrease the absorption of the medications, the effects are of little clinical significance.
	Pyridoxine to prevent neuropathy. Pyridoxine (Vitamin B-6, 25 mg) is recommended for some individuals receiving isoniazid (INH) as part of their treatment regimen to prevent peripheral neuropathy. It should be used in persons at risk for neuropathy (women who are pregnant or breastfeeding or persons with nutritional deficiency, diabetes, HIV infection, renal failure, or alcoholism).

Phase	Principles
Persistent Positive Cultures	**Evaluation when positive cultures persist.** Monitor for culture conversion and promptly evaluate patients with persistently positive cultures after 2 months of therapy to identify the cause. Treatment failure is defined as continued or recurrent positive cultures after 4 months of treatment.
At Completion of Treatment	**Completion in terms of the number of doses.** The criteria for treatment completion are based upon the total number of doses taken and not solely on the duration of therapy.

The Curry International Tuberculosis Center has developed a web presentation on "Practical Solutions for TB Infection Control: Infectiousness and Isolation" available at http://www.currytbcenter.ucsf.edu/tbicweb/

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued "An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy." Consult these recommendations at on pages 943-947 for guidance in the following areas for the safe treatment of LTBI and TB Disease:

- **Program Infrastructure**
  Adopt these standardized approaches to develop safe treatment of LTBI and TB disease.
- **Provider Education and Resources**
  Develop these written resources, educational programs, and referral mechanisms to assure that healthcare providers have the skills, knowledge, and resources to safely diagnose and treat patients with TB disease and LTBI.
- **Pretreatment Clinical Evaluation**
  Refer here for a list of what to include in the pretreatment clinical evaluation and the initial physical examination and when to screen for viral hepatitis.
- **Patient Education**
  Follow these suggestions to improve patients' awareness of and communication about their symptoms of liver disorders. Communicate with patients in their preferred language[3] and carefully confirm that they understand the educational points being made.
- **Medication Administration and Pharmacy**
  Use these tips to distribute antituberculosis medications in ways that encourage and reinforce prompt reporting by patients of adverse effects.
- **Treatment of LTBI and Treatment of TB Disease**
  Use these recommendations to guide treatment decisions and monitoring activities. Numbered lists of recommendations provide detailed information. Three flowcharts show key data and decisions in the following areas: LTBI pretreatment clinical evaluation and counseling, monitoring for hepatotoxicity during LTBI treatment, and monitoring for hepatotoxicity during treatment of TB disease. [46]

Treatment Regimens and Dosages

Use this information to do the following:

- Identify the appropriate regimen
- Determine the appropriate dosage for each drug
- Determine the duration of treatment

The information in this topic was provided using guidelines for treating tuberculosis (TB) that have been developed by the American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC), and Infectious Diseases Society of America (IDSA).

See the "Treatment in Special Situations" (**5.32**) topic in this section of the manual for information on treatment when there is drug-resistant TB, human immunodeficiency virus (HIV) infection, liver disease, or renal disease; when the patient is taking tumor necrosis factor-alpha (TNF-α) antagonists; where there is culture-negative TB or extrapulmonary TB; when the patient is pregnant or breastfeeding; or when the patient is considered to be of pediatric age.

As you use this section, remember the abbreviations for first-line drugs, which are listed below.

TABLE 2: ABBREVIATIONS FOR FIRST-LINE DRUGS

• Ethambutol: EMB • Isoniazid: INH • Pyrazinamide: PZA	• Rifabutin: RFB • Rifampin: RIF • Rifapentine: RPT

Regimens

Identify the appropriate regimen for the patient. There are four basic regimens recommended for treating adults with TB caused by organisms that are known or presumed to be susceptible to isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB). Children, depending on the circumstances, may not receive EMB in the initial phase of a six-month regimen, but the regimens are otherwise identical.

The preferred regimen for treating TB disease consists of an initial two-month phase of four drugs: INH, RIF, PZA, and EMB followed by a four-month continuation phase of INH and RIF.[5]

Each regimen has an initial phase of two months, followed by a choice of several options for a continuation phase of either four or seven months. In Table 3: Drug Regimens for Culture-Positive Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms, the initial phase is denoted by a number (1, 2, 3, or 4), and the options for the continuation phase are denoted by the respective number and a letter designation (a, b, or c).

Directly observed therapy (DOT) is the preferred initial management strategy for all regimens and should be used whenever feasible. All patients being given drugs less than seven days per week (five, three, or two days per week) must receive DOT.

The recommended regimens, and the number of doses specified by each regimen, are described on the next page in Table 3.

For consultation regarding the treatment of TB, consult with the medical provider, local health officer, or WA State TB Services Medical Consultant 206-718-2664.

TABLE 3: DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS[6]

Initial Phase			Continuation Phase			Range of total doses (minimal duration)	Rating* (evidence)†	
Regimen	Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡ § (minimal duration)		HIV–	HIV+
1	INH RIF PZA EMB	Seven days/week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	1a	INH RIF	Seven days/week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk)¶	182–130 (26 wk)	A (I)	A (II)
			1b	INH RIF	Twice weekly for 36 doses (18 wk)	92–76 (26 wk)	A (I)	A (II)#
			1c**	INH RPT	Once weekly for 18 doses (18 wk)	74–58 (26 wk)	B (I)	E (I)
2	INH RIF PZA EMB	Seven days/week for 14 doses (2 wk), then twice weekly for 12 doses (6 wk) or 5 d/wk for 10 doses (2 wk),¶ then twice weekly for 12 doses (6 wk)	2a	INH RIF	Twice weekly for 36 doses (18 wk)	62–58 (26 wk)	A (II)	B (II)#
			2b**	INH RPT	Once weekly for 18 doses (18 wk)	44–40 (26 wk)	B (I)	E (I)
3	INH RIF PZA EMB	Three times weekly for 24 doses (8 wk)	3a	INH RIF	Three times weekly for 54 doses (18 wk)	78 (26 wk)	B (I)	B (II)
4	INH RIF EMB	Seven days/week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	4a	INH RIF	Seven days/week for 217 doses (31 wk) or 5 d/wk for 155 doses (31 wk)¶	273–195 (39 wk)	C (I)	C (II)
			4b	INH RIF	Twice weekly for 62 doses (31 wk)	118–102 (39 wk)	C (I)	C (II)

Definitions of abbreviations: DOT = directly observed therapy; EMB = ethambutol; INH = isoniazid; HIV = human immunodeficiency virus; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; D = should generally not be offered; E = should never be given.

† Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.

‡ When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice.

§ Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.

¶ Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is rated AIII.

Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/microliter.

** Options 1c and 2b should be used only in HIV-negative patients who have negative sputum smears at the time of completion of 2 months of therapy and who do not have cavitation on initial chest radiograph. For patients started on this regimen and found to have a positive culture from the 2-month specimen, treatment should be extended an extra 3 months.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):3.

Dosages

For consultation regarding the treatment of TB, contact the medical provider, local health officer, or WA State TB Services Medical Consultant 206-718-2664.

TABLE 4: DOSES*OF FIRST-LINE ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN[†] [7]

Drug	Preparation	Adults/children	Doses			
			Daily	1x/wk	2x/wk	3x/wk
INH	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml); aqueous solution (100 mg/ml) for intramuscular injection[¶]	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
		Children (max.)	10–15 mg/kg (300 mg)	—	20–30 mg/kg (900 mg)	—
RIF	Capsule (150 mg, 300 mg); powder may be suspended for oral administration; aqueous solution for intravenous injection	Adults[‡] (max.)	10 mg/kg (600 mg)	—	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (max.)	10–20 mg/kg (600 mg)	—	10–20 mg/kg (600 mg)	—

Drug	Preparation	Adults/children	Doses			
			Daily	1x/wk	2x/wk	3x/wk
RFB	Capsule (150 mg)	Adults‡ (max.)	5 mg/kg (300 mg)	__	5 mg/kg (300 mg)	5 mg/kg (300 mg)
		Children	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown
RPT	Tablet (150 mg, film coated)	Adults	__	10 mg/kg (continuation phase) (600 mg)	__	__
		Children	This drug is not approved for use in children	This drug is not approved for use in children	This drug is not approved for use in children	This drug is not approved for use in children
PZA	Tablet (500 mg, scored)	Adults	See Table 5	__	See Table 5	See Table 5
		Children (max.)	15–30 mg/kg (2.0 g)	__	50 mg/kg (2.0 g)	__
EMB	Tablet (100 mg, 400 mg)	Adults	See Table 6	__	See Table 6	See Table 6
		Children§ (max.)	15–20 mg/kg daily (1.0 g)	__	50 mg/kg (2.5 g)	__

Definitions of abbreviations: EMB = ethambutol; FDA = Food and Drug Administration; INH = isoniazid; PZA = pyrazinamide; RFB = rifabutin; RIF = rifampin; RPT = rifapentine.

* Dose per weight is based on ideal body weight. Children weighing more than 40 kg should be dosed as adults.

† For the purposes of this document, adult dosing begins at the age of 15 years.

¶ INH is used, but not FDA-approved, for intravenous administration. For intravenous use of INH, please consult with the Washington State Tuberculosis Program at 360-236-3447.

‡ Dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

§ The drug can likely be used safely in older children but should be used with caution in children less than 5 years of age, in whom visual acuity cannot be monitored. In younger children, EMB at the dose of 15 mg/kg per day can be used if there is suspected or proven resistance to INH or RIF.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):4.

TABLE 5: SUGGESTED PYRAZINAMIDE DOSES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40 TO 90 KILOGRAMS[8]

Interval	Weight (kg)*		
	40–55 kg	56–75 kg	76–90 kg
Daily, mg (mg/kg)	1,000 (18.2–25.0)	1,500 (20.0–26.8)	2,000 † (22.2–26.3)
Thrice weekly, mg (mg/kg)	1,500 (27.3–37.5)	2,500 (33.3–44.6)	3,000 † (33.3–39.5)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	3,000 (40.0–53.6)	4,000 † (44.4–52.6)

* Based on estimated lean body weight.

† Maximum dose regardless of weight.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):5.

TABLE 6: SUGGESTED ETHAMBUTOL DOSES, USING WHOLE TABLETS, FOR ADULTS WEIGHING 40 TO 90 KILOGRAMS[9]

Interval	Weight (kg)*		
	40–55 kg	56–75 kg	76–90 kg
Daily, mg (mg/kg)	800 (14.5–20.0)	1,200 (16.0–21.4)	1,600 † (17.8–21.1)
Thrice weekly, mg (mg/kg)	1,200 (21.8–30.0)	2,000 (26.7–35.7)	2,400 † (26.7–31.6)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	2,800 (37.3–50.0)	4,000 † (44.4–52.6)

* Based on estimated lean body weight.

† Maximum dose regardless of weight.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):5.

Duration of Treatment

Use the treatment algorithm in Figure 1: Treatment Algorithm for Tuberculosis to determine the duration of treatment. The four recommended regimens for treating patients with TB caused by drug-susceptible organisms have a duration of 6 to 9 months. Each regimen has an initial phase of 2 months, followed by a continuation phase of either 4 or 7 months.

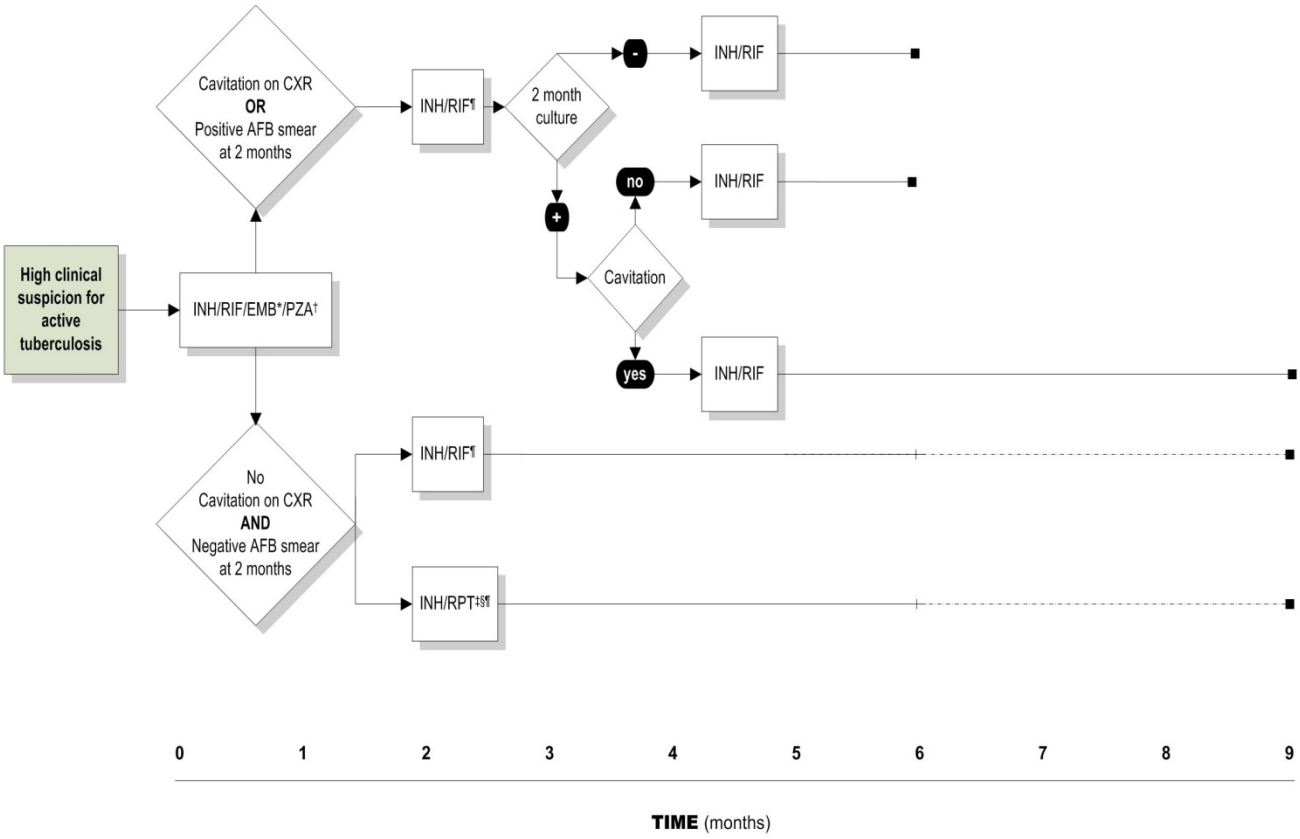
Figure 1 gives directions for treating patients with pulmonary and extrapulmonary TB. The standard duration of treatment for pulmonary TB should be 6 months unless **both** cavitation is present **and** the patient is still culture positive after 2 months, in which case 9 months is recommended. Note that there are 3 exceptions to the standard six-month duration of treatment.

1. For tuberculous meningitis, the optimal length of therapy has not been established, although some experts recommend 9 to 12 months.[10]
2. Treatment for bone or joint TB may need to extend to 9 months.[11]
3. In HIV-negative, culture-negative patients, treatment for four months may be adequate if there is clinical or radiographic improvement and no other etiology identified.[12] However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of 6 months.[13]

The most current TB treatment guidelines state that frequent monitoring of a patient's treatment regimen and response to treatment is critical and can be accomplished through use of a drug-o-gram. This electronic resource provides an interface for entering patient data to create a drug-o-gram. It includes a user's guide with instructions and teaching points. http://www.umdnj.edu/ntbcweb/products/drugogram.htm

To view a sample drug-o-gram form from TPCHD, please see "Drug-O-Gram" located in the **FORMS** section of the manual

FIGURE 1. TREATMENT ALGORITHM FOR TUBERCULOSIS[14]



Definition of abbreviations: AFB = acid-fast bacilli; CXR = chest radiograph; EMB = ethambutol; HIV = human immunodeficiency virus; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

* EMB may be discontinued when results of drug susceptibility testing indicate no drug resistance.

† PZA may be discontinued after it has been taken for 2 months (56 doses).

‡ RPT should not be used in HIV-infected patients with TB or in patients with extrapulmonary TB.

§ Therapy should be extended to 9 months if 2-month culture is positive.

¶ At 2 months, review drug susceptibility and culture results, if applicable, and review these results regularly throughout treatment if the patient is drug resistant.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):6.

Side Effects and Adverse Reactions

The patient should be monitored by a registered nurse and/or clinician or case manager at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be consulted and the patient monitored more frequently. Chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done periodically. See Table 8**:** Monitoring and Interventions for Side Effects and Adverse Reactions.

As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.[15]

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that first-line drugs not be stopped without adequate justification.[16] However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy; whereas with more severe effects, the offending drug or drugs must be discontinued.[17] In addition, proper management of more serious adverse reactions often requires expert consultation.[18] For more information on adverse reactions, see the Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

Basic Monitoring Steps

1. All healthcare workers providing treatment for TB disease should be familiar with the American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines.
   a. All jurisdictions should follow the national monitoring guidelines identified in the current guidelines for treatment of TB, “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.
   b. It is also important to check for guideline updates posted on the CDC’s Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/default.htm and the list of guidelines by date at http://www.cdc.gov/tb/publications/guidelines/default.htm .
2. While on treatment, all patients should be evaluated in person, at baseline (before starting treatment) and then at least monthly for side effects and adverse reactions. For examples of monitoring tools see the Snohomish Drug Interview Sheet, Virginia Clinic Record, Virginia DOT Log and Virginia Vision and Hearing Log in the **Forms** section of this manual.

3. The common side effects of and adverse reactions to drugs used to treat for TB disease are listed below in Table 7: Reporting Reactions to Antituberculosis Medications. Educate patients to stop the medicine and promptly report any of the symptoms or signs listed in Table 7 or any unexplained illness to the prescribing clinic immediately.
   a. If a patient reports a potentially serious adverse reaction, call the patient's medical provider immediately and alert the local health officer or Washington State TB Medical Consultant 206-718-2664.
   b. If a patient reports a potentially less severe side effect, call the patient's medical provider immediately and alert the local health officer or Washington State TB Medical Consultant 206-718-2664 and monitor the patient.
4. If you suspect that an antituberculosis drug may be causing a particular side effect or adverse reaction:
   a. Refer to Table 8: Monitoring and Interventions for Side Effects and Adverse Reactions.
   b. Consult with medical provider, local health officer, or Washington State TB Medical Consultant 206-718-2664.
5. If you suspect that an antituberculosis drug may be interacting with other medications that the patient is taking, refer to pages 45–47 in the "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
6. Document the following patient information:
   a. Review of symptoms, side effects, and adverse reactions (and any labs that were drawn)
   b. Education given
   c. Refill provided
   d. Description of any problems encountered and action taken for that visit
   e. Next appointment

Reporting Reactions

The table below is intended for use by a healthcare worker who performs case management services. The healthcare worker should instruct the patient to report to the provider the side effects and adverse reactions listed below in Table 7.

If a patient reports to a health care worker a potentially serious adverse reaction, the healthcare worker should call the patient's medical provider immediately and alert the local health officer.

If a patient reports to a healthcare worker a potentially less severe side effect, the health care worker should call the patient's medical provider immediately and monitor the patient.

TABLE 7: REPORTING REACTIONS TO ANTITUBERCULOSIS MEDICATIONS[19]

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient's provider. These signs and symptoms suggest side effects, including hepatotoxicity: • Jaundice • Dark urine • Vomiting • Abdominal pain • Fever • Visual changes • Marked clinical rash In consultation with the provider, instruct the patient to stop TB medications until evaluated by the provider.	Report the following signs and symptoms to the patient's provider within 24 hours: • Anorexia • Nausea • Malaise • Peripheral neuropathy: tingling or burning sensation in hands or feet • Rashes More information is available in the Official ATS Statement: Hepatotoxicity of Antibuerculosis Therapy at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf
* These lists are not all-inclusive. Second-line drugs are not included. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]), at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .	

Source: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). TB case management—core components. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. May 11, 1998:9. Available at: http://www.cdph.ca.gov/programs/tb/Documents/TBCB-B-notification-guidelines-2011.pdf, Accessed May 17, 2012.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 8**:** Monitoring and Interventions for Side Effects and Adverse Reactions to do the following:

- Identify the side effects and adverse reactions associated with particular antituberculosis drugs
- Determine how to monitor for side effects and adverse reactions

TABLE 8: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS[20,21,22]

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Isoniazid (INH)	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects	Clinical monitoring monthly Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neurophathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin), and adjust the dose if necessary. More information is available in the Official ATS Statement: Hepatotoxicity of Antibuerculosis Therapy at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (RIF)	• Rash • Gastrointestinal upset • Hepatitis • Fever • Bleeding problems • Thrombocytopenia • Renal failure • Flu-like symptoms • Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to "Section 7: Drug Interactions" on page 45 in "Treatment of Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf . Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC's Division of Tuberculosis "News and Updates" Web page at http://www.cdc.gov/tb/default.htm to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifabutin (RFB)	• Rash • Hepatitis • Fever • Thrombocytopenia • Orange-colored body fluids (secretions, urine, tears) With increased levels of RFB: • Severe arthralgias • Uveitis • Leukopenia	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions Use adjusted daily dose of RFB and monitor for decreased antiretroviral activity and for RFB toxicity if RFB taken concurrently with protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs)	Although drug interactions are less problematic with RFB, they still occur and close monitoring is required. Contraindicated for HIV-infected patients taking hard-gel saquinavir or delavirdine; caution is also advised if RFB is administered with soft-gel saquinavir. Similar to rifampin but less potent of an inducer, rifabutin reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). When used with efavirenz, the daily dose of RFB should be increased from 300 mg to 450 mg or 600 mg. May permanently discolor soft contact lenses.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifapentine (RPT)	Similar to those associated with rifampin	Similar to that for rifampin	Drug interactions involving RPT are being investigated and are likely to be similar to those of rifampin. RPT is an inducer of multiple hepatic enzymes and therefore may increase metabolism of coadministered drugs that are metabolized by these enzymes. For more information, refer to "Section 7: Drug Interactions" on page 45 in "Treatment of Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Pyrazinamide (PZA)	• Gastrointestinal upset • Hepatitis • Rash • Photosensitive dermatitis • Hyperuricemia • Joint aches • Gout (rare)	Clinical monitoring at weeks 2, 4, and 8 If the drug is used in patients with underlying liver disease, laboratory and clinical monitoring should be increased Baseline measurements of uric acid Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, or pregnancy) Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions	Treat hyperuricemia only if patient has symptoms. Might make glucose control more difficult in persons with diabetes. Serum uric acid measurements are not recommended as a routine but may serve as a surrogate marker for compliance.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Ethambutol (EMB)	• Optic neuritis • Rash	Baseline tests of visual acuity (Snellen chart) and color discrimination (Ishihara tests) At each monthly visit, patients should be questioned regarding possible visual disturbances, including blurred vision or scotomata Monthly testing of visual acuity and color discrimination is recommended for • Patients taking doses >15–25 mg/kg • Patients receiving EMB for >2 months • Patients with renal insufficiency	Optic neuritis may be unilateral; check each eye separately. Patients should be instructed to contact their physician or public health clinic immediately if they experience a change in vision. EMB should be discontinued immediately and permanently if there are any signs of visual toxicity.
Rifamate® (INH and RIF) Rifater® (INH, RIF, PZA)	See comments under individual drugs above		

Definitions of abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; EMB = ethambutol; HIV = human immunodeficiency virus; INH = isoniazid; NNRTIs = nonnucleoside reverse transcriptase inhibitors; PZA = pyrazinamide; PIs = protease inhibitors; RFB = rifabutin; RIF = rifampin; RPT = rifapentine.

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49 (No. RR-6):26–29, 38–39; ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):19–25; 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—United States. *MMWR* 2003;52(No. 31):735–736; CDC. Table 6.2: first-line anti-TB medications. In: Chapter 6: treatment of TB disease. *Core Curriculum on Tuberculosis (2011)* [Division of Tuberculosis Elimination Web site]. Updated 2011.Available at: http://www.cdc.gov/tb/education/corecurr/index.htm . Accessed December 21, 2011.

Response to Treatment

For consultation regarding a patient's response to treatment, contact the medical provider, local health officer or WA State TB Services Medical Consultant 206-718-2664.

For patients whose sputum cultures are positive before treatment, the best way to measure the effectiveness of therapy is to obtain specimens for culture at least monthly until the cultures convert to negative. Patients with multidrug-resistant tuberculosis (MDR-TB) should have cultures performed monthly for the entire course of treatment.

In some cases, a patient may not be able to produce a sputum specimen after 2 months of treatment. If the patient has improved clinically and has shown chest radiograph improvement, treatment may be continued as if the patient had a negative sputum specimen at 2 months.

Radiographic evaluations during treatment are of less importance than sputum evaluation. However, a chest radiograph at completion of treatment provides a baseline for comparison with future films.

Patients whose cultures have not become negative or whose symptoms do not resolve despite three months of therapy should be reevaluated for potential drug-resistant disease, as well as for potential failure to adhere to the regimen. If the patient is receiving self-administered therapy, the remainder of treatment should be directly observed.

If drug susceptibility results show resistance to any of the first-line drugs or if the patient remains symptomatic or smear- or culture-positive after 3 months, a tuberculosis (TB) medical expert should be consulted.

In patients with negative sputum cultures before treatment, the major indicators of response to therapy are the chest radiograph and clinical evaluation. The intervals at which chest radiography should be repeated depend on the clinical circumstances and the differential diagnosis that is being considered, but usually should be no more than every three months. If the radiograph does not improve after the patient has received three months of treatment, the abnormality may be the result of either previous (not current) TB or another process.[23]

Completion of Therapy

A full course of therapy (completion of treatment) is determined more accurately if the total number of doses ingested is taken into account, as well as the duration of therapy. If there are no interruptions in drug administration, 6 months is usually the minimum duration of treatment and accurately indicates the amount of time in which drugs are given. However, in human immunodeficiency virus (HIV)-negative, culture-negative patients, treatment for four months may be adequate if there is clinical or radiographic improvement and no other etiology identified.[24]

In some cases, either because of drug toxicity or nonadherence to the treatment regimen, the specified number of doses cannot be administered within the targeted period. In such cases, the goal is to deliver the specified number of doses within a recommended maximum time. For example, for a six-month daily regimen, the total doses should be administered within nine months of beginning treatment. If treatment is not completed within this period, the patient should be assessed to determine the appropriate action to take, such as continuing treatment for a longer duration or restarting treatment from the beginning.

Treating a patient for a defined duration, without accounting for the number of doses taken, can result in under treatment.

Interruptions in treatment may have a significant effect on the duration of therapy. Reinstitution of treatment must take into account the extensiveness of the disease (e.g., cavitary versus noncavitary disease on chest radiograph, smears and cultures, immunologic status), the point in time when the interruption occurred, and the duration of the interruption. In general, the earlier in treatment and the longer the duration of the interruption, the more serious the effect and the greater the need to restart therapy from the beginning.[25]

Post-Treatment Evaluation

Routine follow-up after completion of therapy is not necessary for patients with a satisfactory and prompt bacteriologic response to a six- or nine-month regimen that included both isoniazid and rifampin.

The table below describes the clinician's responsibilities at completion of therapy for cases in which the organisms are drug-susceptible and drug-resistant.

TABLE 9: CLINICIAN'S RESPONSIBILITIES AT COMPLETION OF THERAPY

Drug Susceptibility	Clinician's Actions
Drug-susceptible organisms	Instruct the patient to promptly report the development of any symptoms, particularly prolonged cough, fever, or weight loss.
Organisms resistant to isoniazid, rifampin, or both	Individualize follow-up evaluation.[26]

Treatment in Special Situations

Treatment of tuberculosis (TB) in the following situations requires a high level of expertise or close consultation with an expert to provide appropriate management:

- Drug-resistant TB
- Human immunodeficiency virus (HIV) infection
- Alcoholism
- Liver disease
- Renal insufficiency and end-stage renal disease (ESRD)
- TB associated with tumor necrosis factor-alpha (TNF-α) antagonists
- Culture-negative pulmonary TB
- Extrapulmonary TB
- Pregnancy and breastfeeding
- TB in children

For consultation regarding treatment in the following situations, contact the medical provider, local health officer, or WA State TB Services Medical Consultant 206-718-2664.

Drug-Resistant Tuberculosis

Treatment of TB caused by drug-resistant organisms should be provided by, or in close consultation with, an expert in the management of these difficult situations. Second-line regimens often represent the patient's last hope for being cured, and inappropriate management can have life-threatening consequences.[27]

Drug resistance is proven only by drug-susceptibility testing performed in a competent laboratory. A patient with a strain of *Mycobacterium tuberculosis* resistant to both isoniazid (INH) and rifampin (RIF) has multidrug-resistant TB (MDR-TB). Refer MDR-TB patients immediately to a specialist or seek consultation with a specialized treatment center.[28]

Acquired drug resistance usually develops when an inadequate drug regimen is prescribed (e.g., inappropriate drugs or insufficient dosage) or when there is a combined failure of both the patient and the provider to ensure that an adequate regimen is taken. A patient with acquired drug resistance may transmit his or her strain to others, who may then develop primary drug-resistant TB.[29]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" *(MMWR* 2003;52[No. RR-11]:11-12, 68–70). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. "Multidrug-Resistant" Drug-Resistant Tuberculosis (MDR TB)" (*TB Elimination Fact Sheet;* accessed December 12, 2011). Available at: http://www.cdc.gov/tb/pubs/tbfactsheets/mdrtb.htmhttp://www.cdc.gov/tb/pubs/TBfactsheets.htm .
- CDC. "Extensively Drug-Resistant Tuberculosis (XDR TB)" (*TB Elimination Fact Sheet;* accessed December 12, 2011). Available at: http://www.cdc.gov/tb/publications/factsheets/drtb/xdrtb.htm .

Human Immunodeficiency Virus Infection

Management of HIV-related TB is complex and requires expertise in the management of both HIV disease and TB. Because HIV-infected patients often take numerous medications, some of which interact with antituberculosis medications, clinicians are strongly encouraged to consult with experts who treat HIV-related TB.

It is especially important to use directly observed therapy (DOT) and other adherence-promoting strategies with patients with HIV-related TB.

The following are contraindicated in HIV-infected patients:

- Isoniazid-rifapentine (INH-RPT) once weekly
- Twice-weekly rifampin (RIF)- or rifabutin (RFB)-based regimens in patients with CD4+ cell counts of less than 100 per microliter [30]

Patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations (paradoxical reactions) of TB while receiving antituberculosis treatment.[31]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:9, 50–55). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- ATS, CDC. "Notice to Readers: Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors" (*MMWR* 2004;53[No. 2]:37). Available at: http://www.cdc.gov/mmwr/PDF/wk/mm5302.pdf .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm .

- CDC. "Treatment of Drug-Susceptible TB in HIV-Infected Persons" (*TB Elimination Fact Sheet*; March 2003). Available at: http://www.cdc.gov/tb/publications/factsheets/treatment/treatmentHIVpositive.htm .
- CDC. "Treating Opportunistic Infections Among HIV-exposed and Infected Children" (*MMWR* 2004;53[No. RR-14]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5314.pdf .

Alcoholism

Alcohol-Related Treatment Complications

Risk of drug-induced liver injury and nonadherence complicate health interventions for patients who are diagnosed with TB disease or latent tuberculosis infection (LTBI) and who also are known or suspected to have an alcohol use disorder, who drink heavily, or who regularly consume alcohol.

In several important ways related to tuberculosis and its treatment, alcohol consumption increases health risks and can complicate the treatment of patients.

- **Immunosuppression:** Persons who use alcohol may be at increased risk for acquiring or developing TB, but given the many other potential risk factors that commonly occur among such persons, alcohol use has been difficult to identify as a separate risk factor for TB.[32] However, studies have shown that "alcohol consumption is a major risk factor for infection with opportunistic bacterial, viral, fungal, and parasitic pathogens."[33]
- **Liver injury and death**: Drug-induced liver injury "may occur with all currently recommended regimens for the treatment of …LTBI".[34] In the treatment of TB disease, "the crucial efficacy of isoniazid, and particularly (INH), rifampin, warrants their use and retention, (RIF), and pyrazinamide (PZA), they should be used if at all possible, even in the face of preexisting liver disease."[35] However, it is not fully understood yet how antituberculosis medications cause drug-induced liver injury.[36] For persons taking isoniazid, an association of hepatitis was found with alcohol consumption, with rates being fourfold higher among persons consuming alcohol daily than among those who did not drink alcohol.[37] When a patient has hepatic disease, the risk of drug accumulation and drug-induced hepatitis is increased. However, with more frequent laboratory and clinical monitoring, isoniazid may be used in patients with stable hepatic disease. Transient asymptomatic hyperbilirubinemia may occur in patients taking rifampin or rifapentine, and more severe clinical hepatitis may also occur. Hepatitis is more common when rifampin is given with isoniazid than when rifampin is given alone or with drugs other than isoniazid.[38,39] Pyrazinamide has slightly lower rates of hepatotoxicity than isoniazid or rifampin, but pyrazinamide can cause liver injury that may be severe and prolonged.[40]

To prevent and manage drug-induced liver injury, the American Thoracic Society recommends the following systematic steps: consideration of benefits and risks in selecting patients and regimens, careful and thorough staff and patient education, ready access to care, good communication between providers, and clinical and biochemical monitoring.[41], the most serious common adverse reaction, is defined as a serum aspartate aminotransferase (AST) level more than three times the upper limit of normal in the presence of symptoms or five times the upper limit of normal in the absence of symptoms.

- **Nonadherence to treatment:** Patients who do not complete LTBI treatment risk progression to TB disease, and those who do not complete treatment for TB disease risk relapse, development of drug-resistant TB, serious illness, and possible death. Barriers to adherence may be patient related, such as conflicting health beliefs, alcohol or drug dependence, or mental illness, or they may be system related, such as lack of transportation, inconvenient clinic hours, and lack of interpreters.[42] It is more difficult for patients who have an alcohol use disorder to adhere to therapy. In a prospective study of 224 patients, "noncompliance was significantly associated with homelessness and alcoholism."[43] In a study of 237 patients in the Russian Federation undergoing DOTS treatment for TB disease, "substance abuse was identified as the only factor that was strongly associated with non-adherence…These results suggest that DOTS programmes [sic] might be more likely to achieve TB control targets if they include interventions aimed at improving adherence by diagnosing and treating substance abuse concurrently with standard TB therapy."[44] DOTS programs that have explicitly offered substance abuse treatment have reported better outcomes that those that have not.[45] In South Carolina, joint treatment programs to treat patients with TB who have alcohol and substance abuse problems were used in conjunction with incentives, enablers, and a process of increasing restrictions (health department warnings, then court-ordered directly observed therapy, then involuntary confinement) as needed to address noncompliance. This combination of strategies was associated with an increase in overall completion of antituberculosis therapy and a decrease in new cases between 1986-1991.[46]

Liver Disease

Management of TB in patients with unstable or advanced liver disease is difficult. The likelihood of drug-induced hepatitis may be greater in these patients. The implications of drug-induced hepatitis for patients with marginal hepatic reserve are potentially serious, even life-threatening. Also, fluctuations in the biochemical indicators of liver function (with/without symptoms) related to the preexisting liver disease confound monitoring for drug-induced hepatitis.[47]

For all patients with preexisting liver disease, frequent clinical and laboratory monitoring should be performed to detect drug-induced hepatic injury.[48]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:11, 65). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

Renal Insufficiency and End-Stage Renal Disease

Treatment Complications

Renal insufficiency complicates the management of TB because some antituberculosis medications are cleared by the kidneys. Management may be further complicated by the removal of some antituberculosis agents via hemodialysis. Thus, some alteration in dosing antituberculosis medications is commonly necessary in patients with renal insufficiency and end-stage renal disease (ESRD) receiving hemodialysis.

Dosing Recommendations

Dosing recommendations are based on patients' creatinine clearance.

Administration of drugs that are cleared by the kidneys is managed in the same manner, with an increase in dosing interval for patients having a creatinine clearance of less than 30 ml/minute or for patients receiving hemodialysis.

In patients having a reduced creatinine clearance (but not less than 30 ml/minute), standard doses should be used, but measurement of serum concentrations should be considered to avoid toxicity. [49]

Dosing Recommendations

For patients having a creatinine clearance of less than 30 ml/minute or for patients receiving hemodialysis, the following adjustments to conventional dosing are recommended.

Table 10: DOSING RECOMMENDATIONS FOR ADULT PATIENTS WITH REDUCED RENAL FUNCTION AND FOR ADULT PATIENTS RECEIVING HEMODIALYSIS[50]

Drug	Change in Frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg 3 times per week
Rifampin	No change	600 mg once daily, or 600 mg 3 times per week
Pyrazinamide	Yes	25–35 mg/kg per dose 3 times per week (not daily)
Ethambutol	Yes	15–25 mg/kg per dose 3 times per week (not daily)
Moxifloxacin	No	400 mg/dose daily†
Levofloxacin	Yes	750–1,000 mg per dose 3 times per week (not daily)

Drug	Change in Frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis
Cycloserine	Yes	250 mg once daily, or 500 mg/dose 3 times per week*
Ethionamide	No change	250-500 mg/dose daily
p-Aminosalicylic acid	No change	4 g/dose, twice daily
Streptomycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Capreomycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Kanamycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Amikacin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)

* The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity. (See Section 3 of the "Treatment of Tuberculosis" guidelines.)

† No adjustment in dose is needed for those with low creatinine clearance or those on hemodialysis. No adjustment in dosing frequency is needed, but it may be given three times per week to facilitate administration.

Standard doses are given unless there is intolerance. The medications should be given after hemodialysis on the day of hemodialysis. Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.

Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing, using serum concentration monitoring.

Source: Resources

ATS, CDC, IDSA. "Treatment of Tuberculosis." (MMWR 2003;52(No.2003;52[No. RR-11): 64; with information on Moxifloxacin added by Dr. Charles DaleyRR-11]:10–11, 63–65) http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

- **Rifampin** and **isoniazid** are metabolized by the liver, so conventional dosing may be used in the setting of renal insufficiency.
- Supplemental dosing is not necessary for **isoniazid, rifampin,** or **ethambutol**. If **pyrazinamide** is given after hemodialysis, supplemental dosing is not required.
- A longer interval between doses with three times a week administration is recommended for **pyrazinamide** and **ethambutol**.
- Doses of **streptomycin, kanamycin, amikacin,** and **capreomycin** must be adjusted in patients with renal failure, and the dosing interval should be increased. In general, the

dose should not be reduced because the drugs exhibit concentration dependent bactericidal action, and smaller doses may reduce drug efficacy.

- **Ethionamide** requires no dose adjustment.
- Twice daily dosing (4 g) of **p-Aminosalicylic acid (PAS)** should be adequate if the granule formulation is used. Its metabolite, acetyl-PAS, is substantially removed by hemodialysis.
- **Cycloserine** requires an increase in the dosing interval to avoid accumulation between hemodialysis sessions, and the drug should be given after hemodialysis to avoid underdosing.
- The **fluoroquinolones** undergo some degree of renal clearance that varies from drug to drug. For example, levofloxacin undergoes greater renal clearance than moxifloxacin. It should be noted that the fluoroquinolone dosing recommendations for end-stage renal disease provided by the manufacturers were developed for treating pyogenic bacterial infections. These recommendations may not be applicable to the treatment of tuberculosis in patients with end-stage renal disease.

Administration of Drugs Immediately After Hemodialysis

Administration of all antituberculosis drugs immediately after hemodialysis will facilitate DOT (three times per week) and avoid premature removal of the drugs.

Monitoring of Serum Drug Concentrations

It is important to monitor serum drug concentrations in persons with renal insufficiency who are taking cycloserine, ethambutol, or any of the injectable agents to minimize dose-related toxicity, while providing effective doses.

Clinicians also should be aware that patients with end-stage renal disease may have additional clinical conditions, such as diabetes mellitus with gastroparesis, that may affect the absorption of the antituberculosis drugs, or they may be taking concurrent medications that interact with these drugs. Under these circumstances a careful clinical and pharmacologic assessment is necessary, and, in selected cases, serum drug concentration measurements may be used to assist in determining the optimum dose of the antituberculosis drugs.

Finally, data currently do not exist for patients receiving peritoneal dialysis. Because the drug removal mechanisms differ between hemodialysis and peritoneal dialysis, it cannot be assumed that all of the recommendations in Table 1 will apply to peritoneal dialysis. Such patients may require close monitoring, including measurements of the serum concentrations of the antituberculosis drugs.[51]

Tuberculosis Associated with Tumor Necrosis Factor-Alpha Antagonists

TB is a potential consequence of treatment with tumor necrosis factor-alpha (TNF-α) antagonists such as the following:

- Infliximab (Remicade®)
- Etanercept (Enbrel®)
- Adalimumab (Humira®)

These drugs work by blocking TNF-α, an inflammatory cytokine, and are approved for treating rheumatoid arthritis and other selected autoimmune diseases. Blocking TNF-α can allow TB disease to emerge from latent TB infection (LTBI). Healthcare providers should take steps to prevent TB in immunocompromised patients and remain vigilant for TB as a cause of unexplained febrile illness.[52]

Patients should be screened for risk factors for *M. tuberculosis* infection and tested for infection before initiating immunosuppressive therapies, including TNF-α antagonists.[53]

Resources

- CDC. "Tuberculosis Associated with Blocking Agents against Tumor Necrosis Factor-Alpha—California, 2002–2003" (*MMWR* 2004;53[No. 30]:83–686). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5330a4.htm .

Culture-Negative Pulmonary Tuberculosis

A diagnosis of TB should not be ruled out if *M. tuberculosis* cannot be isolated from persons suspected of having pulmonary TB on the basis of clinical features and chest radiographic examination. Alternative diagnoses should be carefully considered and further appropriate diagnostic studies undertaken in persons with apparent culture-negative TB.[54]

A diagnosis of culture-negative pulmonary TB can be made if all the following conditions are met:

- Initial acid-fast bacilli (AFB) smears and cultures are negative.
- Clinical or radiographic response occurs within 2 months of initiation of therapy.
- No other diagnosis has been established.[55]

After the initial phase (first 2 months), continue treatment with an additional 2 months of isoniazid and rifampin during the continuation phase to complete a total of 4 months of treatment.[56] However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of 6 months.[57]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:10, 61). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

Extrapulmonary Tuberculosis

The basic principles for treating pulmonary TB also apply to extrapulmonary forms of the disease. The addition of corticosteroids is recommended for patients with TB pericarditis and TB meningitis. Recommendations concerning duration of therapy are as follows:

- Use a six-month course of therapy for TB involving any site.[58] **Exceptions:** For bone or joint TB, use a six- to nine-month regimen.[59] For the meninges, use a nine- to twelve-month regimen.[60]
- Consider prolonging therapy for patients with TB in any site that is slow to respond.[61]

Note: Affected lymph nodes may enlarge while patients are receiving appropriate therapy or after treatment has ended without any evidence of bacteriological relapse. On occasion, new nodes can appear during or after treatment as well.[62]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:10, 56–61). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- Division of Tuberculosis Elimination. *Fact Sheets* (Division of Tuberculosis Elimination Web site; accessed February 2007). Available at: http://www.cdc.gov/tb/publications/factsheets/default.htm .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 2008). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm .

Pregnancy and Breastfeeding

Because of the risk of TB to the fetus, treatment in pregnant women should be initiated whenever the probability of maternal disease is moderate to high. The initial treatment regimen should consist of isoniazid (INH), rifampin (RIF), and ethambutol (EMB). As pyrazinamide (PZA) generally is not included in the initial treatment regimen, the minimum duration of therapy is nine months. Although these drugs cross the placenta, they do not appear to have teratogenic effects.

Breastfeeding should not be discouraged in women being treated with first-line antituberculosis agents because the small concentrations of drugs in breast milk do not produce toxicity in the nursing newborn. Conversely, drugs in breast milk should not be considered an effective treatment for TB in a nursing infant.[63]

Pyridoxine supplementation (25 mg/day) is recommended for all women taking INH who are either pregnant or breastfeeding.[64]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:11, 62–63). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 2008). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm .
- Red Book Plus 27th Edition, American Academy of Pediatrics, 2006. Available at http://www.aapredbook.org.

Tuberculosis in Children

A pediatric patient is a person below the age of 18 years.

Because of the high risk of disseminated TB in infants and children younger than 5 years of age, treatment should be started as soon as the diagnosis of TB is suspected.[65]

The following recommendations have been developed for children:

- Regimens recommended for infants, children, and adolescents with TB are generally the same as those for adults.
  Exception: Ethambutol (EMB) is not used routinely in children.[66]
- Duration of treatment in children is 6 months.
  Exception: For disseminated disease and TB meningitis, use a nine- to twelve- month regimen.[67] For other exceptions, refer to "Duration of Treatment" in the "Treatment Regimens and Dosages" topic in this section.
- DOT should always be used in treating children.[68]

Due to the difficulty of isolating *M. tuberculosis* in a child with pulmonary TB, the choice of drugs for the child is frequently guided by the drug susceptibility test results of the presumed source case. If drug-resistant TB is suspected or the source case isolate is not available, specimens for microbiological evaluation should be obtained via early morning gastric aspiration, bronchoalveolar lavage, or biopsy.[69]

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:9–10, 55–56). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
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- Consent and Treatment Plan (Georgia)
- DOT Log (Virginia)
- Drug Interview Sheet (SHD)
- Drug-O-Gram (TPCHD)
- LTBI and Disease (Kansas)
- Medication Administration Record (MAR)
- Medication Information (Georgia)
- Medication Log
- QFT: TB Control Guidelines for Public Health Staff (Thurston County)
- Protocol and Standing Orders (SHD)
- Symptom Screen (Georgia)
- Tuberculosis Screening Guidelines

Quick Start Check List: Treatment of Latent Tuberculosis Infection

This check list is designed to assist public health nurses in treating a patient for latent tuberculosis infection. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
Diagnose latent tuberculosis infections (LTBI), ruling out tuberculosis (TB) disease	Instructions: • Diagnosis of Latent Tuberculosis Infection (6.3) • Protocol and Standing Orders (SHD) • Symptom Screen (Georgia) • LTBI and Disease (Kansas) • Chart Audit Tool
Select and appropriate treatment regimen: ☐ Assure that an appropriate treatment regimen, dosages, and duration are selected ☐ Assure that these special situations are considered: • Human immunodeficiency virus (HIV) infection • Alcoholism • Pregnancy and breastfeeding	Instructions: • Regimens (7.11 Table 1) • Dosages (7.12 Table 2) • Consent and Treatment Plan (Georgia)
Monitor the patient regularly: ☐ Assure that the patient is assessed at least monthly for • Clinical follow-up • Adherence to LTBI treatment • Adverse reactions to LTBI treatment	Instructions: • Reporting Reactions (7.15 Table 3) • Monitoring and Interactions (7.17 Table 4) The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Persons Being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm Forms • Drug Interview Sheet (SHD) • Clinic Record (Virginia) • Medication Information (Georgia) • Medication Administration Record • Medication Log
Confirm the completion of treatment: ☐ Verify completion of treatment 6 to 9 months after treatment was started depending upon • Regimen • Adherence	Instructions: • Recommended Regimens (7.21 Table 5)

To understand the evaluation process in diagnosing TB disease and LTBI, view the "Tuberculosis Screening Guidelines" provided on page 4.6.

Introduction

Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Determine whom to treat for latent tuberculosis infection (LTBI)
- Select appropriate treatment regimens and dosages
- Monitor patients for adverse reactions
- Monitor patients' adherence to treatment
- Determine whether and when therapy is completed
- Provide treatment in special situations, such as when a patient is pregnant or has tuberculosis (TB)–human immunodeficiency virus (HIV) coinfection

Prevention of TB has major public health implications, so it is essential to identify and treat all those with risk factors for TB disease.[1] LTBI is the presence of *Mycobacterium tuberculosis* organisms (tubercle bacilli), with no symptoms and no radiographic or bacteriologic evidence of TB disease.[2] A person with LTBI is noninfectious but can develop active TB disease. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions associated with an increased risk for the progression of LTBI to TB disease.

To control and prevent TB, our healthcare resources and efforts in Washington State should be directed to meet the priorities outlined in the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America." One of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification and treatment of persons with LTBI at risk for progression to TB.[3]

Targeted tuberculin testing for LTBI is a strategic component of TB control that identifies persons at high risk for developing TB who would benefit by treatment of LTBI, if detected. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions that are associated with an increased risk for progress of LTBI to active TB.

Healthcare providers must communicate the risks and benefits of treatment to their patients and encourage adherence and treatment completion. Treatment of LTBI is an essential element in controlling and eliminating TB in the United States. LTBI treatment substantially reduces the risk that TB infection will progress to disease.[4] Depending upon adherence and length of treatment, completing treatment for LTBI can reduce the risk of TB disease by 65–90%.[5]

Whom to Treat

Determine whom to treat for latent tuberculosis infection (LTBI). Certain groups are at high risk of developing tuberculosis (TB) disease once infected, so make every effort to begin appropriate treatment and to ensure that these persons complete the entire course of treatment for LTBI.[6]

For a list of high-risk groups by tuberculin skin test (TST) results, see the Tuberculin Skin Test Results listings, which follow in this topic. For more information on targeted testing, see "Targeted Testing for Latent Tuberculosis Infection" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see the "Time Frames for Contact Investigation" topic in the Contact Investigation section of the manual (**9.16**) and "Guidelines for Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Several treatment regimens are available for the treatment of LTBI, and providers should discuss treatment options with their patients.[7]

For more information on treatment of LTBI, see the "Treatment Regimens and Dosages" topic in this section of the manual (**7.9**) and Treatment of Latent Tuberculosis Infection (LTBI) at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

LTBI Card: Patient's TB Testing and Treatment Record, available at http://www.umdnj.edu/globaltb/products/ltbicard.htm.

Susceptible and Vulnerable Contacts

A contact is someone who has been exposed to *M. tuberculosis* infection by sharing air space with a person with infectious TB.[8] Susceptible contacts are those who are more likely to become ill with TB disease if they are infected, and vulnerable contacts are those who could suffer severe morbidity if they progress to TB disease.[9] (These include children under 5 years of age, and those who are HIV-infected, immunocompromised or have other underlying disease processes.) Persons who are susceptible and/or vulnerable to TB disease are candidates for window period treatment, which is administering treatment for presumptive TB infection during the interval between infection and detectable skin test or positive IGRA testing. The National Tuberculosis Controllers Association (NTCA) and the CDC recommend that the window period be estimated at 8 to 10 weeks.[10] The following contacts with initially negative TST or IGRA test results should receive treatment for LTBI after TB disease has been ruled out by clinical examination and chest radiograph:

1. Contacts younger than 5 years of age (with highest priority given to those under 3 years)
2. Contacts with human immunodeficiency virus (HIV) infection or who are otherwise immunocompromised

If the second skin test or IGRA result is negative and the contact is immunocompetent (including immunocompetent young children) and no longer exposed to infectious TB, treatment for LTBI may be discontinued, and further follow-up is unnecessary. If the second test is negative but the contact is immunocompromised (e.g., with human immunodeficiency virus [HIV] infection), a course of therapy for LTBI should be completed. If the second test result is negative but the person remains in close contact with an infectious patient, treatment for LTBI should be continued if the contact is:

1. Less than 5 years old.
2. Aged 5–15 years, at the clinician's discretion.
3. HIV-seropositive or otherwise immunocompromised.[11]

Persons known to be (or suspected of being) immunocompromised, such as HIV-infected persons, should be given treatment for LTBI regardless of the TST or IGRA reaction.[12]

For more information regarding the IGRA, QuantiFERON®--TB Gold, see CDC, NTCA. "Guidelines for the investigation of contacts of persons with infectious tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf, and "Guidelines for using the QuantiFERON®- -TB Gold test for detecting Mycobacterium tuberculosis infection, United States", MMWR 2005;54(no. RR-15) at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

Also, see more information on this topic in QFT: TB Control Guidelines for Public Health Staff (FORMS), and "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf.

Tuberculin Skin Test Results of 5 mm or More

Persons in the following high-risk groups are candidates for treatment of LTBI if their skin test result is 5 mm or more:

- Persons with HIV infection
- Recent contacts of persons with newly diagnosed infectious TB
- Persons with fibrotic changes on their chest radiograph that are consistent with old TB
- Persons with organ transplants and other immunosuppressed patients (receiving the equivalent of 15 mg or more/day of prednisone for at least one month)[13]

Tuberculin Skin Test Results of 10 mm or More

Persons in the following high-risk groups are candidates for treatment of LTBI if their skin test result is greater than or equal to 10 mm:

- Foreign-born persons who have recently arrived (within five years) from countries with a high TB incidence or prevalence, or persons who have recently traveled to these countries (most countries in Africa, Asia, Latin America, Eastern Europe, and Russia (formerly the USSR)
- Persons who are alcoholics, who inject drugs, or who use other high-risk substances, such as crack cocaine
- Residents and employees of high-risk congregate settings, such as correctional institutions, homeless shelters, long-term residential care facilities (e.g., nursing homes, mental institutions), hospitals, and other healthcare facilities
- Mycobacteriology laboratory personnel
- Persons with medical conditions or undergoing treatments that increase the risk of TB disease (diabetes mellitus, silicosis, recent infection with *M. tuberculosis* within the past two years, bone marrow and organ transplant recipients, prolonged high-dose corticosteroid therapy and other immunosuppressive therapy, chronic renal failure, hemodialysis, some hematological disorders [e.g., leukemias and Hodgkin's disease], other specific malignancies [e.g., carcinoma of the head, neck, or lung], chronic malabsorption syndromes, weight of 10% or more below ideal body weight, and intestinal bypass or gastrectomy)
- Children less than 5 years of age
- Infants, children, and adolescents exposed to adults at high risk for developing TB disease
- Locally identified groups at high risk[14]

Tuberculin Skin Test Results of 15 mm or More[15]

Persons in the following groups may be considered for treatment of LTBI if their skin test result is greater than or equal to 15 mm. These groups should be given a lower priority for prevention efforts than the groups already listed above.

- Persons with no known risk factors for TB disease
- Healthcare workers* who are otherwise at low risk for TB disease and who received baseline testing at the beginning of employment as part of a TB screening program[16]

Treatment Regimens and Dosages

Select appropriate treatment durations, regimens, and dosages. Treatment of latent tuberculosis infection (LTBI) is an essential part of the strategy to eliminate tuberculosis (TB) in the United States. Persons with LTBI who are considered at increased risk for TB should be offered treatment.[17]

There are several treatment regimens available for the treatment of LTBI, and providers should discuss options with patients. Persons who are at especially high risk for TB, and either are suspected of nonadherence or are on an intermittent dosing regimen, should be treated using directly observed therapy (DOT). This method of treatment is especially appropriate when a household member is on DOT for TB disease or in institutions and facilities where a staff member can observe treatment.

For a list of high-risk groups, see “Targeted Testing for Latent Tuberculosis Infection” at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see “Treatment of Latent Tuberculosis Infection (LTBI)” at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

The most current TB treatment guidelines state that frequent monitoring of a patient's treatment regimen and response to treatment is critical and can be accomplished through use of a drug-o-gram. This electronic resource provides an interface for entering patient data to create a drug-o-gram. It includes a user's guide with instructions and teaching points. http://www.umdnj.edu/ntbcweb/products/drugogram.htm

To view a sample drug-o-gram form from TPCHD, please see “Drug-O-Gram” located in the **FORMS** section of the manual.

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued "An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy." Consult these recommendations at on pages 943-947 for guidance in the following areas for the safe treatment of LTBI and TB Disease:

- **Program Infrastructure**
  Adopt these standardized approaches to develop safe treatment of LTBI and TB disease.
- **Provider Education and Resources**
  Develop these written resources, educational programs, and referral mechanisms to assure that healthcare providers have the skills, knowledge, and resources to safely diagnose and treat patients with TB disease and LTBI.
- **Pretreatment Clinical Evaluation**
  Refer here for a list of what to include in the pretreatment clinical evaluation and the initial physical examination and when to screen for viral hepatitis.
- **Patient Education**
  Follow these suggestions to improve patients' awareness of and communication about their symptoms of liver disorders. Communicate with patients in their preferred language[18] and carefully confirm that they understand the educational points being made.
- **Medication Administration and Pharmacy**
  Use these tips to distribute antituberculosis medications in ways that encourage and reinforce prompt reporting by patients of adverse effects.
- **Treatment of LTBI and Treatment of TB Disease**
  Use these recommendations to guide treatment decisions and monitoring activities. Numbered lists of recommendations provide detailed information. Three flowcharts show key data and decisions in the following areas: LTBI pretreatment clinical evaluation and counseling, monitoring for hepatotoxicity during LTBI treatment, and monitoring for hepatotoxicity during treatment of TB disease.19

Regimens

Identify an appropriate regimen for the patient using the national guidelines provided in Table 1 below.

TABLE 1: RECOMMENDED DRUG REGIMENS FOR TREATMENT OF LATENT TUBERCULOSIS INFECTION IN ADULTS[20]

Drug	Interval and Duration	Comments	Rating* (evidence)†	
			HIV–	HIV+
INH	Daily for 9 months‡ §	In HIV-infected patients, INH may be administered concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs).	A (II)	A (II)
	Twice weekly for 9 months‡ §	DOT must be used with twice-weekly dosing.	B (II)	B (II)
INH	Daily for 6 months§	This duration of therapy is not indicated for HIV-infected persons, those with fibrotic lesions on chest radiographs, or children.	B (I)	C (I)
	Twice weekly for 6 months§	DOT must be used with twice-weekly dosing.	B (II)	C (I)
RIF	Daily for 4 months in adults Daily for 6 months in children	RIF is used for persons who are contacts of patients with INH-resistant, RIF-susceptible TB. Some antiretroviral drugs, such as the protease inhibitors and NNRTIs, have interactions with the rifamycins. Clinicians should consult Web-based updates or experts for the latest specific recommendations. The optimal length of RIF therapy in children with LTBI is not known; however, the American Academy of Pediatrics recommends 6 months of treatment.[21]	B (II)	B (III)

Definitions of abbreviations: DOT = directly observed therapy; HIV = human immunodeficiency virus; INH = isoniazid; LTBI = latent tuberculosis infection; RIF = rifampin.

* Strength of recommendation: A = Preferred, B = Acceptable alternative, C = Offer when A and B cannot be given.

† Quality of evidence: I = Randomized clinical trial data, II = Data from clinical trials that are not randomized or were conducted in other populations, III = Expert opinion.

‡ Recommended regimen for children <18 years of age.

§ Recommended regimen for pregnant women.

Source: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):31.

The regimen of rifampin (RIF) and pyrazinamide (PZA) for two months is no longer recommended for treatment of LTBI because of its association with severe liver injury. For more information, see the CDC's "Update: Adverse Event Data and Revised American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection" (*MMWR* 2003;52[No. 31]:735) at http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf

Dosages

Once the appropriate regimen has been identified, refer to Table 2 for instructions on dosages for each drug. The information in Table 2 is taken from ATS, CDC, and Infectious Diseases Society of America (IDSA) guidelines.

TABLE 2: RECOMMENDED DOSAGES[22,23]

Drug	Preparation	Adults/ Children	Daily	Twice a Week
INH	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml)	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)
		Children (max.)	10–15 mg/kg (300 mg)	20–30 mg/kg (900 mg)
RIF	Capsule (150 mg, 300 mg); powder may be suspended for oral administration	Adults (max.)	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (max.)	10–20 mg/kg (600 mg)	10–20 mg/kg (600 mg)
Definitions of abbreviations; INH = isoniazid; RIF = rifampin.				

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):4; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):28–29.

The use of INH elixir is discouraged, as it commonly causes diarrhea and cramping in children. If children have difficulty taking medications, open capsules and crush tablets, and then hide the drugs in soft foods or liquids. Possible foods include maple syrup, hot fudge, Nutella, apple sauce, jams and jellies, spinach baby food, and chocolate whipped cream, etc. Layer the food and drug on a spoon, and teach the child to take the contents of the spoon without chewing.[24]

For consultation regarding the treatment of LTBI in persons who have been in contact with a case who is resistant to drugs in the recommended regimens, you may contact the WA State TB Services Medical Consultant 206-718-2664.

Side Effects and Adverse Reactions

The patient should be monitored by a registered nurse and/or clinician or case manager at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be consulted and the patient monitored more frequently. Blood chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done periodically. See Table 4: Monitoring and Interventions for Side Effects and Adverse Reactions in this section.

As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.[25]

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that the drugs with the highest evidence rating not be stopped without adequate justification.[26] However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy; whereas with more severe effects, the offending drug or drugs must be discontinued.[27] In addition, proper management of more serious adverse reactions often requires expert consultation.[28] A comprehensive statement on Hepatoxicity of Antituberculosis Therapy has been published by the American Thoracic Society, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

Basic Monitoring Steps

1. All healthcare workers providing treatment for latent tuberculosis infection (LTBI) should be familiar with the American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines.
   - **a.** All jurisdictions should follow the national monitoring guidelines identified in the current treatment guidelines for treatment of LTBI, “Targeting Tuberculin Testing and Treatment of Latent Tuberculosis Infection,” pages 26–29 at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .
   - **b.** It is also important to check for guideline updates posted on the CDC’s Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/default.htm and the list of guidelines by date at http://www.cdc.gov/tb/publications/guidelines/default.htm.
2. While on treatment, all patients should be evaluated in person, at baseline (before starting treatment), and then at least monthly for side effects and adverse reactions. For sample monitoring forms, please see the Snohomish Drug Interview Sheet, Clinic Record (Virginia), and DOT Log (Virginia) in the **Forms** section of this manual.

3. The common side effects of and adverse reactions to drugs used to treat for LTBI are listed in Table 3: Reporting Reactions to Antituberculosis Medications. Educate patients to stop the medicine and promptly report any of the symptoms or signs listed in Table 3 or any unexplained illness to the prescribing clinic immediately.
   a. If a patient reports a potentially serious adverse reaction, call the patient's provider immediately and take action according to the provider's instructions.
   b. If a patient reports a potentially less severe side effect, call the patient's provider immediately and monitor the patient.
4. If you suspect that an antituberculosis drug may be causing a particular side effect or adverse reaction:
   a. Refer to Table 4: Monitoring and Interventions for Side Effects and Adverse Reactions below.
   b. Consult with the patient's medical provider, Local Health Officer or WA State TB Services Medical Consultant (206) 718-2664.
5. If you suspect that an antituberculosis drug may be interacting with other medications that the patient is taking, refer to pages 45–47 in the "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.
6. Document the following patient information:
   a. Review of symptoms, side effects, and adverse reactions (and any labs that were drawn)
   b. Education given
   c. Refill provided
   d. Description of any problems encountered and action taken for that visit
   e. Next appointment

For more information on Assessing and Managing the Risk of Liver Disease in the Treatment of LBTI, please see the algorithm at: http://www.heartlandntbc.org/products/assessing_and_managing_the_risk_of_liver_disease_in_the_treatment_of_ltbi.pdf

Reporting Reactions

The table below is intended for use by a healthcare worker who performs case management services. The healthcare worker should instruct the patient to report to the provider the side effects and adverse reactions listed in Table 3.

If a patient reports to a healthcare worker a potentially serious adverse reaction, the healthcare worker should call the patient's provider immediately and take action according to the provider's instructions.

If a patient reports to a healthcare worker a potentially less severe side effect, the healthcare worker should call the patient's provider immediately and monitor the patient.

TABLE 3: REPORTING REACTIONS TO ANTITUBERCULOSIS MEDICATIONS[29]

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient's provider. These signs and symptoms suggest side effects, including hepatotoxicity: • Jaundice • Dark urine • Vomiting • Abdominal pain • Fever • Visual changes • Marked clinical rash In consultation with the provider, instruct the patient to stop TB medications until evaluated by the provider.	Report the following signs and symptoms to the patient's provider **within 24 hours**: • Anorexia • Nausea • Malaise • Peripheral neuropathy: tingling or burning sensation in hands or feet • Rashes
* These lists are not all-inclusive. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf,	

NOTE: The two-month regimen of rifampin and pyrazinamide is no longer recommended due to serious and fatal hepatitis associated with this regimen.[30]

At present, the Division of Tuberculosis Elimination (DTBE) urges health departments, hospices, hospitals, jails, prisons, and private medical offices to report all severe adverse events (e.g., liver injury, pancreatitis, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for LTBI that occurred after January 1, 2004, to DTBE by calling 404-639-8401. Also, if not done previously, please call the Washington State Tuberculosis Services at 360-236-3443 to report these severe adverse events.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 4**:** Monitoring and Interventions for Side Effects and Adverse Reactions to do the following:

- Identify the side effects and adverse reactions associated with particular antituberculosis drugs
- Determine how to monitor for side effects and adverse reactions

TABLE 4: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS[31,32,33]

Antituberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Isoniazid (INH)	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects	Clinical monitoring monthly Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin), and adjust the dose if necessary. More information is available in the Official ATS Statement: Hepatotoxicity of Antibuerculosis Therapy, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Antituberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (RIF)	• Rash • Gastrointestinal upset • Hepatitis • Fever • Bleeding problems • Thrombocytopenia • Renal failure • Flu-like symptoms • Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to "Section 7: Drug Interactions" on page 45 in "Treatment of Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf . Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC's Division of Tuberculosis "News and Updates" Web page at http://www.cdc.gov/tb/default.htm to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Adherence

Monitor patients for adherence to self-administered latent tuberculosis infection (LTBI) treatment regimens at least monthly throughout treatment.[34] It is difficult to identify who will and who will not be adherent.[35] If patients do not take medicine as directed, the effectiveness of the regimen decreases, and the patient will be at greater risk of progressing to disease in the future and of infecting others.

Monthly Assessment of Adherence

At each visit, the clinician should assess adherence by doing the following:

1. Ask patients how many doses they have missed since their last refill. If patients are asked, "Did you take all your pills last month?" the natural inclination is to say "yes" even if they did not.
2. Have patients bring their bottle of medicine to the refill appointment, and count how many pills are left.
3. If adherence problems are identified, include patients in the problem-solving process.
   a. Ask patients why they think that doses are missed and what could be done better: change the time of day, the location where they keep or take their pills, etc.
   b. Find out if there are barriers to obtaining refills in a timely manner that could be corrected.
   c. Review with patients what they believe is their risk of developing tuberculosis (TB) if medicine is not taken. Provide education again, as needed.
   d. Mutually agree upon a plan to improve adherence.
   e. Praise patients for cooperation.
4. If adherence seems to be good, praise patients.

For information on what to include in a patient education session, see the Patient Education section of the manual (15.1)

Directly Observed Therapy

Patients in the following high-risk groups are strongly recommended for directly observed therapy (DOT).

- DOT is mandatory for any intermittent regimen.
- DOT is strongly encouraged for those with the greatest risk for progression to tuberculosis (TB) disease:
  - Young children who are recent contacts to infectious cases.
  - Human immunodeficiency virus (HIV)-infected persons.

For more information, see the "Directly Observed Therapy/Videophone DOT" topic in the Case Management section of the manual (**8.51**).

For more information on adherence strategies for different developmental stages, see Appendix C in the New Jersey Medical School National Tuberculosis Center's *Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider* (New Jersey Medical School Global Tuberculosis Institute Web site; 2009) at http://www.umdnj.edu/ntbcweb/products/mgmtltbi.htm

Completion of Therapy

Determine whether and when therapy is completed based upon the total number of doses administered, not on the duration of therapy. When patients have had lapses in therapy but are still able to complete the recommended number of doses in the allotted time period, encourage them to complete therapy.

Assess patients who will not complete appropriate therapy within the time frame specified to determine whether or not to restart treatment. If the decision is made to retreat the patient, then **restart** the entire regimen and follow the recommended treatment plan of therapy. Specific factors to consider when determining whether to restart treatment include the following:

- Individual's risk for developing tuberculosis (TB) disease
- Total number of doses of latent tuberculosis infection (LTBI) treatment administered
- Time elapsed since the last dose of treatment for LTBI
- Patient adherence issues (previous attempts at completion, willingness to continue, etc.)

Give nonadherent patients who are at very high risk of developing TB disease every opportunity to complete treatment for LTBI. Consider these patients for intermittent therapy with directly observed therapy (DOT), and evaluate the use of incentives and enablers.[36]

Treatment of LTBI in contacts is considered a priority in TB control activities. Make every effort to assure completion of treatment in contacts.

All contacts who are being treated for infection should be seen face-to-face by a healthcare provider at least monthly. Incentives and enablers are recommended as aids to adherence, and the healthcare provider should educate the patient about TB, its treatment, and the signs of adverse drug effects at each patient encounter.[37]

Table 5 describes the duration of therapy and the number of doses that patients are required to take to complete therapy as well as the time frame within which the total number of doses must be administered for completion of therapy.

TABLE 5: RECOMMENDED REGIMENS FOR COMPLETION OF THERAPY[38]

Regimen	Age	Duration of Therapy	Number of Doses	Must be Administered Within
INH daily	Adult and child	9 months	270	12 months
INH daily	Adult	6 months	180	9 months
INH twice weekly	Adult and child	9 months	76	12 months
INH twice weekly	Adult	6 months	52	9 months
RIF daily	Adult	4 months	120	6 months
	Child	6 months	180	9 months
Definitions of abbreviations: INH = isoniazid; RIF = rifampin.				

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):26–27; CDC. Regimens. In: Chapter 6: treatment of LTBI. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: http://www.cdc.gov/tb/education/corecurr/index.htm. Accessed January 10, 2012.

Make every effort to encourage patients to adhere to the LTBI treatment regimen. However, if a patient has failed three attempts to complete treatment, no further effort may be merited. The healthcare provider should contact patients who interrupt therapy and are at high risk of developing TB disease (for example, contacts of patients with infectious TB, human immunodeficiency virus (HIV)-infected patients, or TB Class 4 patients) for reevaluation.[39]

Treatment in Special Situations

Treatment of latent tuberculosis infection (LTBI) in the following situations requires special consideration:

- Human immunodeficiency virus (HIV) infection
- Alcoholism

Human Immunodeficiency Virus and Latent Tuberculosis Infection

Treatment of latent tuberculosis infection (LTBI) in a person with human immunodeficiency virus (HIV) infection can be extremely complicated. Consultation is available through the WA State TB Services Medical Consultant 206-718-2664.

HIV infection is the strongest known risk factor for the progression of LTBI to tuberculosis (TB) disease. HIV-infected persons with LTBI are 100 times more likely to progress to TB disease than are those patients without HIV infection. Coinfected HIV and LTBI patients have a 7 to 10 percent *yearly* risk of developing TB disease. Patients with only LTBI have a 10 percent *lifetime* risk of developing TB disease.

High-risk contacts (less than 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Resources

- CDC. "TB Guidelines: HIV/AIDS" (DTBE Web site; accessed February 2007). Available at: http://www.cdc.gov/tb/publications/guidelines/HIV_AIDS.htm .
- ATS, CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]:33). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .
- CDC. "Prevention and Treatment of Tuberculosis among Patients Infected with Human Immunodeficiency Virus: Principles of Therapy and Revised Recommendations" (*MMWR* 1998;47(No. RR-20). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4720.pdf .
- CDC. "Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors" (*MMWR* 2000;49[No. 9]:185). Available at: http://www.cdc.gov/mmwr/PDF/wk/mm4909.pdf .

Alcoholism

Alcohol-Related Treatment Complications

Risk of drug-induced liver injury and nonadherence complicate health interventions for patients who are diagnosed with TB disease or latent tuberculosis infection (LTBI) and who also are known or suspected to have an alcohol use disorder, who drink heavily, or who regularly consume alcohol.

In several important ways related to tuberculosis and its treatment, alcohol consumption increases health risks and can complicate the treatment of patients.

- **Immunosuppression:** Persons who use alcohol may be at increased risk for acquiring or developing TB, but given the many other potential risk factors that commonly occur among such persons, alcohol use has been difficult to identify as a separate risk factor for TB.[40] However, studies have shown that "alcohol consumption is a major risk factor for infection with opportunistic bacterial, viral, fungal, and parasitic pathogens."[41]
- **Liver injury and death**: Drug-induced liver injury "may occur with all currently recommended regimens for the treatment of …LTBI".[42] In the treatment of TB disease, "the crucial efficacy of isoniazid, and particularly (INH), rifampin, warrants their use and retention, (RIF), and pyrazinamide (PZA), they should be used if at all possible, even in the face of preexisting liver disease."[43] However, it is not fully understood yet how antituberculosis medications cause drug-induced liver injury.[44] For persons taking isoniazid, an association of hepatitis was found with alcohol consumption, with rates being fourfold higher among persons consuming alcohol daily than among those who did not drink alcohol.[45] When a patient has hepatic disease, the risk of drug accumulation and drug-induced hepatitis is increased. However, with more frequent laboratory and clinical monitoring, isoniazid may be used in patients with stable hepatic disease. Transient asymptomatic hyperbilirubinemia may occur in patients taking rifampin or rifapentine, and more severe clinical hepatitis may also occur. Hepatitis is more common when rifampin is given with isoniazid than when rifampin is given alone or with drugs other than isoniazid.[46,47] Pyrazinamide has slightly lower rates of hepatotoxicity than isoniazid or rifampin, but pyrazinamide can cause liver injury that may be severe and prolonged.[48]
- To prevent and manage drug-induced liver injury, the American Thoracic Society recommends the following systematic steps: consideration of benefits and risks in selecting patients and regimens, careful and thorough staff and patient education, ready access to care, good communication between providers, and clinical and biochemical monitoring.[49], the most serious common adverse reaction, is defined as a serum aspartate aminotransferase (AST) level more than three times the upper limit of normal in the presence of symptoms or five times the upper limit of normal in the absence of symptoms.

- **Nonadherence to treatment:** Patients who do not complete LTBI treatment risk progression to TB disease, and those who do not complete treatment for TB disease risk relapse, development of drug-resistant TB, serious illness, and possible death. Barriers to adherence may be patient related, such as conflicting health beliefs, alcohol or drug dependence, or mental illness, or they may be system related, such as lack of transportation, inconvenient clinic hours, and lack of interpreters.[50] It is more difficult for patients who have an alcohol use disorder to adhere to therapy. In a prospective study of 224 patients, "noncompliance was significantly associated with homelessness and alcoholism."[51] In a study of 237 patients in the Russian Federation undergoing DOTS treatment for TB disease, "substance abuse was identified as the only factor that was strongly associated with non-adherence…These results suggest that DOTS programmes [sic] might be more likely to achieve TB control targets if they include interventions aimed at improving adherence by diagnosing and treating substance abuse concurrently with standard TB therapy."[52] DOTS programs that have explicitly offered substance abuse treatment have reported better outcomes that those that have not.[53] In South Carolina, joint treatment programs to treat patients with TB who have alcohol and substance abuse problems were used in conjunction with incentives, enablers, and a process of increasing restrictions (health department warnings, then court-ordered directly observed therapy, then involuntary confinement) as needed to address noncompliance. This combination of strategies was associated with an increase in overall completion of antituberculosis therapy and a decrease in new cases between 1986-1991.[54]

For more information, see "Tuberculosis Infection Control Program Model Policies for Chemical Dependency Treatment Agencies in Washington State," available at http://www.dshs.wa.gov/pdf/dbhr/certforms/TBPolicy.pdf

Pregnancy and Breastfeeding

Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progression to disease. Pregnant women should be targeted for testing only if they have a specific risk factor for LTBI or for progression of LTBI to disease.

Extensive use of INH during pregnancy has shown that, although it readily crosses the placental barrier, the drug is not teratogenic, even when given during the first four months of gestation. However, in the absence of risk factors (HIV infection or recent contact to infectious case), wait until after the woman has delivered to avoid administering unnecessary medication during pregnancy. There is potential for an increased risk of hepatotoxicity during pregnancy and the first 2-3 months of the post-partum period. Consider delaying treatment for LTBI until 2-3 months post-partum. Supplementation with 10-25mg/d of pyridoxine (vitamin B6) is recommended.

Breastfeeding is not contraindicated when the mother is being treated for LTBI. However, breastfeeding mothers taking INH and their nursing infants should receive supplemental

pyridoxine. Note that the amount of INH provided by breast milk is inadequate for treatment of the infant.[55]

Resources

- Red Book Plus 27th Edition, American Academy of Pediatrics, 2007. Available at http://www.aapredbook.org.

Resources and References

Resources

Whom to Treat

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .
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- American Academy of Pediatrics. Pickering LK ed. Red Book: 2007 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL; American Academy of Pediatrics 2007: http://aapredbook.aappublications.org/

Treatment Regimens and Dosages

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .
- CDC. "Update: Adverse Event Data and Revised American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection" (*MMWR* 2003;52[No. 31]). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm .
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Side Effects and Adverse Reactions

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]:26–29, 38–39). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf.
- National Tuberculosis Controllers Association–National Tuberculosis Nurse Consultant Coalition. *Tuberculosis Nursing: A Comprehensive Guide to Patient Care* (Atlanta, GA;1997:47–51, 63–64).
- CDC. Module 4: "Treatment of Tuberculosis and Tuberculosis Infection" (*Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web Site]; 2008:. Available at: http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf.
- Saukkonen, J. Et al. An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy. Am J Respir Crit Care Med. 2006:174, 935-952. Available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Adherence

- CDC. Module 9: "Patient Adherence to Tuberculosis Treatment" (S*elf-Study Modules on Tuberculosis.* Division of Tuberculosis Elimination Web Site; 1999). Available at: http://www.cdc.gov/tb/education/ssmodules/module9/ss9contents.htm .

  This module is entirely devoted to assessing and promoting adherence. It covers the many areas that need to be addressed, such as:

  - Case management: assigning responsibility to the healthcare worker
  - Communication and problem-solving skills
  - Education of the patient
  - Using interpreters when needed
  - Using incentives (rewards) and enablers (things that remove barriers for patients)
  - Using directly observed therapy (DOT)
- CDC. *Improving Patient Adherence to Tuberculosis Treatment.* (1994)
- National Tuberculosis Controllers Association–National Tuberculosis Nurse Consultant Coalition. *Tuberculosis Nursing: A Comprehensive Guide to Patient Care* (Atlanta, GA; 1997:69–84).

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DOH 343-071 June 2012
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Diagnosis of Latent Tuberculosis Infection

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Forms Used in this Section

- Chart Audit Tool
- Contact Investigation
- Contact Investigation Instructions
- Drug-O-Gram (TPCHD)
- LTBI Testing/Recording
- Protocol and Standing Orders (SHD)
- QFT: TB Control Guidelines for Public Health Staff (Thurston County)
- Symptom Screen (Georgia)
- Tuberculosis Screening Guidelines

Quick Start Check List: Diagnosis of Latent Tuberculosis Infection

This check list is designed to assist public health nurses in evaluating a patient for latent tuberculosis infection. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
Determine whom to test • Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks	Instructions: For persons who are not part of a contact investigation: Targeted Tuberculin Testing • http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf Mantoux Tuberculin Skin Test • http://cdc.gov/tb/education/mantoux/default.htm For persons who are contacts: Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5414.pdf • Symptom Screen (Georgia) • Protocol and Standing Orders (SHD) Forms: • Contact Investigation o Instructions
Conduct tuberculin skin testing: • Place and measure tuberculin skin tests (TST's) • Interpret TSTs: • 5 mm is positive for persons who are contacts or immunosuppressed • 10 mm is positive for persons with recent infection or clinical conditions of increased risk • 15 mm is positive for persons at low risk • Skin test conversion: For persons previously skin tested, an increase in induration of 10 mm or more within a two-year period is classified as a conversion to positive	Instructions: Mantoux Tuberculin Skin Test • http://www.cdc.gov/tb/education/Mantoux/default.htm • Mantoux Tuberculin Skin Test (manual) (6.9) • Candidates for Mantoux Tuberculin Skin Test (6.10) For diagnosis of latent TB infection (LTBI), improved blood tests called interferon gamma release assays (IGRAs) are available. IGRAs (10.23) are available in Washington State. • IGRA (10.23) • QFT: TB Control Guidelines for Public Health Staff (Thurston County) • LTBI Testing/Recording

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
Conduct tuberculin skin testing (cont): ☐ A positive reaction to tuberculin in a bacille Calmette-Guérin-vaccinated person indicates infection with Mycobacterium tuberculosis when the person tested • Is a contact of another person who has infectious tuberculosis (TB) • Resided in a country with high prevalence of TB • Had continuous exposure to populations in which the prevalence of TB is high	Instructions: The CDC has released "Severe Isoniazid- Associated Liver Injuries Among Persons being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm Review the "Tuberculosis Infection Control Program Model Policies for Chemical Dependency Treatment Agencies in Washington State," available at http://www.dshs.wa.gov/pdf/dbhr/certforms/TBPolicy.pdf Forms: • Chart Audit Tool
Screen for human immunodeficiency virus (HIV) in the following persons who test positive with TST or IGRA: • Screen all persons in the following groups: • Persons at risk for HIV • Persons younger than 5 years, or • Persons who have a clinical condition such as silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemia's and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of greater than 10% body weight, gastrectomy and jejunoileal bypass	Instructions: • Targeted Tuberculin Testing http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf
Exclude active pulmonary disease: • Obtain chest radiographs for patients with positive TST results. Chest radiographs are indicated for all persons being considered for treatment of latent TB infection (LTBI)	
Determine whether to treat the patient for LTBI	Instructions: • Targeted Tuberculin Testing http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf
Follow up patients who are contacts in a contact investigation	Instructions: • Contact Investigation Guidelines http://www.cdc.gov/mmwr/pdf/rr/rr5414.pdf
Assure that all persons with abnormal chest x-rays and/or symptoms of TB disease are evaluated for TB disease ☐ Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks	Instructions: Targeted Tuberculin Testing • http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf Forms: • Contact Investigation o Instructions

To understand the evaluation process in diagnosing TB disease and LTBI, view the "Tuberculosis Screening Guidelines" provided on page **4.6.**

Introduction

Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Classify patients with latent TB infection (LTBI)
- Diagnose LTBI

In the 2005 guideline "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification of persons with LTBI at risk for progression to TB disease, and treatment of those persons with an effective drug regimen.[1]

Contacts are mentioned within this section, but their evaluation and follow-up are covered in more depth in the Contact Investigation section of the manual (**9.1**). For information on treatment, refer to the Treatment of Latent Tuberculosis Infection section of the manual (**7.1**).

High-Risk Groups

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or for progression to TB disease. Persons in the high-risk groups listed in Table 1: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease are candidates for tuberculin skin testing.

Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country who is also infected with HIV infection is at a much higher risk of having or developing active TB than a US-born individual with HIV infection.

TABLE 1: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE[2]

For Tuberculosis (TB) Infection	For Progression to TB Disease[3]

• High-priority contacts such as housemates or coworkers, or contacts of persons who have smear-positive pulmonary or laryngeal tuberculosis (TB)
• Infants, children, and adolescents exposed to adults in high-risk categories
• Recent immigrants (primarily <5 years) from countries with high incidence of TB (Asian, African, Latin American, and Eastern European countries have TB rates 5–30 times higher than U.S. rates, and an increasing percentage of TB cases in the United States are occurring among immigrants from those countries)
• Residents and employees of high-risk congregate settings (e.g., correctional institutions, nursing homes and other long-term care facilities providing care to high-risk residents and clients, and homeless shelters)
• Some healthcare workers who serve high-risk clients, especially emergency departments, staff involved in high-risk procedures, and laboratories manipulating TB cultures
• Some high-risk racial or ethnic minority populations, defined locally as having an increased prevalence of TB (in Washington State this group includes American Indians and Alaskan Natives)
• Some medically underserved, low-income populations as defined locally (e.g., homeless, transient populations)
• Persons who inject illicit drugs; any other locally identified high-risk substance abuse users
	• Persons with HIV infection
	• Infants and children aged <5 years
	• Persons infected with *Mycobacterium tuberculosis* within the previous 2 years
	• Persons with a history of untreated or inadequately treated TB disease
	• Persons with radiographic findings consistent with previous TB disease
	• Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine)
	• Persons with any of the following clinical conditions or other immunocompromising conditions:
	  • Silicosis
	  • Diabetes mellitus
	  • End-state renal disease (ESRD)/chronic renal failure, hemodialysis
	  • Some hematologic disorders (e.g., leukemia's and lymphomas)
	  • Other malignancies (e.g., carcinoma of head, neck, or lung)
	  • Body weight ≥10% below ideal body weight
	  • Prolonged corticosteroid use
	  • Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF-α] antagonists)
	  • Organ transplantation
	  • Gastrectomy
	  • Chronic malabsorption syndromes
	  • Jejunoileal bypass

Source: Adapted from: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9. Also, Tuberculosis Infection Control: A Practical Manual for Preventing TB http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12

Diagnosis of Latent Tuberculosis Infection

The diagnosis of latent tuberculosis infection (LTBI) has traditionally been based upon results of tuberculin skin testing. However, the QuantiFERON®-TB Gold (QFT-G) test, QuantiFERON®-TB Gold in-tube (QFT™) test and the -SPOT®.*TB* test, which are whole-blood interferon gamma release assays (IGRAs), are now other options for detecting LTBI.

Use the Mantoux tuberculin skin test (TST) or an IGRA to test for *Mycobacterium tuberculosis* infection. IGRA can be used in all circumstances in which the TST is used, and IGRAs usually can be used in place of (and not in addition to) the TST.[4]

For information on testing methods available in Washington refer to the Laboratory Services Section (**10.1**)

For a summary of the TB classification numbers, refer to the "Tuberculosis Classification System" topic in the Surveillance section.

Interferon Gamma Release Assays (IGRA)

Blood assay for *Mycobacterium tuberculosis* (BAMT) is a general term referring to recently developed in vitro diagnostic tests that assess for the presence of infection with *M. tuberculosis*. This term includes, but is not limited to, interferon gamma release assays (IGRAs). The IGRAs currently approved by the Food and Drug Administration (FDA) and available on the market are the QuantiFERON®-TB Gold in-tube (QFT™) test, which replaces the QuantiFERON®-TB Gold (QFT-G) test and the -SPOT®.*TB* test. IGRAs can be used in all circumstances in which the TST is used, and the IGRAs usually can be used in place of the TST.[5] Other cytokine-based immunoassays are under development and may also become useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products, in combination with Centers for Disease Control and Prevention (CDC)-issued recommendations, may provide additional diagnostic alternatives.[6]The advantages of IGRA, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory, the variability associated with skin test reading can be eliminated. [7] In addition, IGRA tests appear to be less affected by past bacille of Calmette-Guérin (BCG) vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results. [8] However, the IGTA tests have practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. For the QFT-G test, the blood must arrive at the laboratory less than 12 hours after collection to be incubated with the test antigens, while the lymphocytes are viable.[9] For a QFT™ test, the blood specimens are collected directly into the three blood collection tubes, shaken vigorously, and then incubated at the collection site. After incubation, blood collection tubes should be stored no longer than three days prior to centrifugation and laboratory manipulation.

A single IGRA test is used in place of (and not in addition to) the TST in screening of healthcare workers.

Resources for IGRA Testing:

- CDC. "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC" (*MMWR* 2005;54[No. RR-15]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf .
- CDC. "Guidelines for Using the QuantiFERON-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States" (*MMWR* 2005;54[No. RR-15]). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.htm .
- CDC. "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf .
- Curry International Tuberculosis Center. *Tuberculosis Infection Control: A Practical Manual for Preventing TB* (Curry International Tuberculosis Center web site; 2007). Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12
- CDC Interferon Gamma Release Assays (IGRA) guidelines, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" *(MMWR* 2010; 59 [No. RR-5];1-25) at http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf.

  CDC Interferon-Gamma Release Assays (fact sheet) that will assist you in learning more about IGRAs. http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm

For information on available IGRA testing in Washington refer to the Laboratory Services Section (**10.8**)

For more information regarding QFT healthcare worker guidelines see QFT: TB Control Guidelines for Public Health Staff (Forms Section)

Find answers to common questions posed by healthcare professionals on the use of QFT at http://www.cellestis.com/IRM/Company/ShowPage.aspx?CPID=1588&EID=60701344

Mantoux Tuberculin Skin Testing (TST)

The Mantoux method of tuberculin skin testing is used to detect infection with *Mycobacterium tuberculosis.*

In general, it may take up to 10 weeks after infection for a person to develop a delayed-type immune response to tuberculin which is measurable with the Mantoux tuberculin skin test (TST).[10] During the test, tuberculin is injected intradermally into the skin. The immune system of most persons with tuberculosis (TB) infection will recognize the tuberculin, causing a reaction in the skin. Repeated TSTs do not produce hypersensitivity. Guidelines for interpretation of the TST are found in the CDC Mantoux Tuberculin Skin Test Training Materials Kit at http://www.cdc.gov/tb/education/mantoux/default.htm

The size of the measured induration (a hard, dense, raised formation) and the patient's individual risk factors should determine whether TB infection is diagnosed.[11] Based upon the sensitivity and specificity of the purified protein derivative (PPD) TST and the prevalence of TB in different groups, three cut-points have been recommended for defining a positive tuberculin reaction:

- Greater than or equal to 5 mm on induration
- Greater than or equal to 10 mm induration
- Greater than or equal to 15 mm of induration[12]

For more information on cut-points for the TST, see the "Interpretation of the Tuberculin Skin Test" topic in this section of the manual (**6.16**), or Mantoux Tuberculin Skin Test Training Materials Kit at http://www.cdc.gov/tb/education/mantoux/default.htm

Candidates for Mantoux Tuberculin Skin Testing

The Mantoux TST can be administered to all persons, including pregnant women,[13] persons who have previously been vaccinated with bacille Calmette-Guérin (BCG),[14] and human immunodeficiency virus (HIV)-infected persons. However, persons with a documented prior positive TST do not need another TST, and the Mantoux TST should not be administered until four weeks after vaccination with live-virus vaccines.

If the person being tested is a contact, follow the procedures outlined in the Contact Investigation section of the manual (**9.1**) and Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Pregnancy

Tuberculin skin testing is entirely safe and reliable for pregnant women, and pregnant women at high risk for TB infection or disease should be tested. Screen pregnant women for TB infection if they have any of the following conditions:

- Symptoms suggestive of TB disease
- HIV infection
- Behavioral risk factors for HIV
- Medical conditions other than HIV infection that increase the risk for TB disease
- Close contact with a person who has pulmonary or laryngeal TB disease
- Immigration from an area of the world where incidence of TB is high

Bacille Calmette-Guérin Vaccine

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis.* Because their effectiveness in preventing infectious forms of TB has never been demonstrated in the United States, they are not recommended as a TB control strategy in the United States, except under rare circumstances. They are, however, used commonly in other countries. A history of BCG vaccination is not a contraindication for tuberculin skin testing, nor does it influence the indications for a TST. Administer and measure TSTs in BCG-vaccinated persons in the same manner as in those with no previous BCG vaccination.

Bacille Calmette-Guérin Talking Points

1. Tuberculin reactivity caused by BCG vaccination wanes with time but can be boosted with a TST.[15]
2. There is no method to distinguish TB tuberculin reactions caused by vaccination with BCG from those caused by mycobacterial infections.[16]
3. A diagnosis of M. tuberculosis infection should be considered for any BCG-vaccinated person who has TST reaction ≥10 mm of induration.[17]
4. Treatment for LTBI should be considered for a person who is TST positive and has had previous BCG vaccination if the person is:
   - A contact of a person with infectious TB or
   - Vaccinated and born in or resided in a country of high prevalence of TB or
   - Exposed to persons at risk for TB[18]
5. BCG vaccination should be considered for infants and children who reside in high morbidity countries to prevent meningeal TB.[19]
6. There is no scientific evidence of protective ability of BCG for preventing pulmonary TB in adolescents or adults.[20]
7. An IGRA is preferred for testing persons who have received BCG. [21]

The BCG vaccine is not available in the United States. The Vancouver Chest Clinic [655 W. 12th Ave., Vancouver, B.C. phone (604) 660-6108] will provide a BCG vaccine. The client must: a) call for an appt., b) get a baseline TST, c) if TST is negative a medical provider will interview the client and if the client meets their criteria, the medical provider will approve the BCG vaccine.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with TST for HIV-infected persons in the United States.[22]

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that cause an impaired cellular immune system include HIV infection, severe or febrile illness, measles or other viral infections, Hodgkin's disease, sarcoidosis, live-virus vaccination, and corticosteroid or immunosuppressive therapy. Persons with conditions such as these may have suppressed reactions to a TST even if infected with TB. However, there are no simple skin testing protocols that can reliably identify persons as either anergic or nonanergic and that have been proven to be feasible for application in public health TB screening programs. Factors limiting the usefulness of anergy skin testing include the following:

- Problems with standardization and reproducibility
- Low risk for TB associated with a diagnosis of anergy
- Lack of apparent benefit of treatment for LTBI in groups of anergic HIV-infected persons

For more information on Anergy testing, see http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

Also, see JAMA article "The Case Against Anergy Testing as a Routine Adjunct to Tuberculin Skin Testing", at http://jama.ama-assn.org/cgi/content/abstract/283/15/2003?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=The+Case+Against+Anergy+Testing+as+a+Routine+Adjunct+to+Tuberculin+Skin+Testing&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT

Documented Prior Positive Tuberculin Skin Test

Persons who have tested positive in the past and can provide documentation of their status should not have another TST. Instead, they should have a TB symptom assessment questionnaire administered to identify any symptoms of TB disease.[23] Persons who are symptomatic should have a chest radiograph performed. See Tuberculosis Infection Control: A Practical Manual for Preventing TB (appendix E. TB Screening Questionnaire for Healthcare Workers).

Live-Virus Vaccines

The Mantoux TST can be administered in conjunction with all vaccines. However, the measles (MMR) vaccine—and possibly mumps, rubella, varicella, and live attenuated influenza vaccines—may transiently suppress the response to PPD.[24] Therefore, if a vaccine containing live virus (e.g., measles, smallpox) has already been given, the TST should be deferred until (or repeated) at least four weeks after the vaccine was administered.

When giving the TST and the MMR, one of the following three sequences should be used:

- Apply the TST at same visit as the MMR
- Delay the TST at least four weeks if the MMR is given first
- Apply the TST first and then give the MMR when the TST is measured[25]

American Academy of Pediatrics. Pickering LK ed. Red Book: 2003 Report of the Committee on Infectious Diseases. 26th ed. Elk Grove Village, IL; American Academy of Pediatrics 2003: http://aapredbook.aappublications.org/content/dtl/2003/1/

Administration of the Tuberculin Skin Test

The TST should be placed and read by a healthcare worker who has received appropriate training and is following written protocols.

TABLE 2: BEFORE YOU BEGIN TO ADMINISTER A TUBERCULIN SKIN TEST

Before You Begin to Administer a TST	
Review Information	CDC. *Mantoux Tuberculin Skin Test Facilitator Guide at* http://www.cdc.gov/tb/education/mantoux/default.htm Follow all Infection control procedures (including hand washing before and after the procedure and the use of gloves and a sharps container)

Gather Equipment	• Gloves • Alcohol pads or alternative skin cleanser • Safety needle • Tuberculin syringe (Do not pre-draw tuberculin into syringes prior to test.) • Purified protein derivative (PPD) (Tubersol® or Aplisol®: See the warning in the text below in this table.) • Sharps container Note: Date PPD tuberculin vials when opened and discard after 30 days. See the package insert for appropriate storage information.

Read the PPD labels carefully before administering a TST. The packaging of tetanus toxoid-containing vaccines (TTCVs) is similar to Tubersol® and Aplisol®, and all are refrigerated. See the CDC's "Errors Involving Mix-up of Tuberculin Purified Protein Derivative and Vaccine Products" (*TB Notes Newsletter*. 2005;No. 1).

How to Administer a Tuberculin Skin Test

1. Obtain the patient's written consent if required by the provider's agency/institution
2. Inject air into the vial air space (not into the solution). Injection of air into the air space in the vial prevents creation of negative pressure within the vial, allowing the antigen to be withdrawn easily. Injecting air into the solution creates bubbles and may interfere with withdrawing the correct amount of antigen.[26]The injection should be placed on the palm-side-up surface of the forearm, about two to four inches below the elbow. Your local institutional policy may specify the right or left forearm for the skin test. The area selected should be free of any barriers to placing and reading the skin test, such as muscle margins, heavy hair, veins, sores, tattoos, or scars.
3. After choosing the injection site, clean the area with an alcohol swab by circling from the center of the site outward. Allow the site to dry completely before giving the injection.
4. Using a disposable tuberculin safety needle and syringe, inject 0.1 ml of PPD tuberculin containing 5 tuberculin units (TU) intradermally with the needle bevel facing upward. Because some of the tuberculin solution can adhere to the inside of the plastic syringe, the skin test should be given as soon as possible after the syringe is filled.
5. The injection should produce a discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter. **Note:** If a 6- to10-mm wheal is not produced, repeat the test on the opposite arm or the same arm, 2 inches from the original site.
6. Record the date and time of TST administration, location of injection site, dose, name of person who administered the test, the name and manufacturer of the tuberculin product used, lot number, expiration date, and reason for testing. [21]

Measurement of the Tuberculin Skin Test

A trained healthcare worker should read the TST 48 to 72 hours after the intradermal injection. Patients should never be allowed to read their own TSTs.[22]

- A positive reaction can be measured anytime after 48 hours.
- If the results appear negative and more than 72 hours have passed, the test should be repeated. It can be repeated immediately or one to three weeks later if two-step testing is required for employment.

Refer to the topic entitled "Two-Step Tuberculin Skin Testing" in the Infection Control section of the manual (**11.13**) and Guidelines for Preventing Transmission of Mycobacterium Tuberculosis in Health-Care Settings at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

Before you measure a TST, review information in the CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* at http://www.cdc.gov/tb/education/mantoux/default.htm

How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm (from the thumb side of the arm to the little finger side of the arm or vice versa).
2. Induration is a hard, dense, raised formation. Measure only induration hardness and not swelling around the site of the injection. Do **not** measure erythema (redness). A TST with erythema, but no induration, is a negative TST (nonreactive.)
3. Record the test result in mm, not as "positive" or "negative." An exact reading in mm may be necessary to interpret whether conversions occur on a subsequent test. Record a TST with no induration as "0 mm." Where there is induration, do not round off the reading, but record it exactly as read.
4. Report adverse reactions to a TST (e.g., blistering, ulcerations, necrosis) to the FDA's MedWatch Program at 1-800-FDA-1088, or via the Internet at http://www.fda.gov/Safety/MedWatch/default.htm

Interpretation of the Tuberculin Skin Test

TSTs should be interpreted by a trained healthcare worker. Use Table 3 below to interpret TSTs.

Call the local health jurisdiction regarding TST reactions when interpretation and medical follow-up are unclear.

Before you interpret a TST, review information in the CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* at http://www.cdc.gov/tb/education/mantoux/default.htm .

How to Interpret a Tuberculin Skin Test

Use the table below to determine when a reaction is positive.

TABLE 3: POSITIVE TUBERCULIN SKIN TEST REACTIONS

Induration Size	Considered Positive For:
5 mm or more	• Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) • Recent contacts to an infectious case of tuberculosis (TB) disease • Persons with fibrotic lesions on chest radiograph consistent with healed TB • Persons with organ transplants or other immunosuppressed persons (such as those receiving the equivalent of >15 mg/day of prednisone for >1 month) • Persons receiving treatment with tumor necrosis factor-alpha (TNF-α) antagonists
10 mm or more	• Foreign-born persons recently arrived (within 5 years) from countries with a high TB incidence or prevalence (e.g., most countries in Africa, Asia, Latin America, Eastern Europe, the former USSR, or from refugee camps) • Persons who inject drugs or use other high-risk substances, such as crack cocaine • Alcoholics • Residents and employees in high-risk, congregate settings (e.g., correctional institutions; long-term residential care facilities, such as nursing homes, mental institutions, etc.; hospitals and other healthcare facilities; homeless shelters; and refugee camps) • Mycobacteriology laboratory personnel • Persons with other medical conditions that increase the risk of TB disease • Children younger than 5 years of age, or children and adolescents exposed to adults in high-risk categories
15 mm or more	• Persons with no known risk factors for TB

When interpreting TST results, be aware of the following:

Skin test conversions: For persons previously skin tested, an increase in induration of 10 mm or more within a two-year period is classified as a conversion to positive.

False-negative reactions may be due to the following:

- Anergy

See “Anergy Testing” (**6.11**) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual and Guidelines for Preventing Transmission of Mycobacterium Tuberculosis in Health-Care Settings at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

- Recent TB infection (within the past 8 weeks) since the TST may not yet show positive
- Very young age (less than 6 months of age, because the immune system is not fully developed)
- Overwhelming TB disease
- Vaccination with live viruses (e.g., measles, mumps, rubella, varicella, oral polio, or yellow fever).

TB skin testing should be done either on the same day as vaccination with live virus or at least four weeks after vaccination.

See “Live-Virus Vaccines” (**6.12**) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual.

- Some viral infections (measles, mumps, chickenpox, or HIV)
- Corticosteroids or other immunosuppressive agents given for two or more weeks

False-positive reactions may be due to the following:[23]

- Nontuberculous mycobacteria (NTM) or mycobacterium other than tuberculosis (MOTT)
- BCG vaccination

See “Bacille Calmette-Guérin Vaccine” (**6.10**) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual.

Human Immunodeficiency Virus Screening

Voluntary counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. HIV counseling and testing has also been recommended for contacts of persons with TB.[27]

The Centers for Disease Control and Prevention (CDC) recommends the following:

- HIV screening for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
- Routine HIV testing for persons suspected of having TB disease and contacts to TB patients
- Persons at high risk for HIV infection should be screened for HIV at least annually[28]

Follow-Up Activities

After testing, complete the following tasks

If the person has signs or symptoms of TB, evaluate for TB disease as described in the "Diagnosis of Tuberculosis Disease" topic in the Diagnosis of Tuberculosis Disease section of the manual (**4.1**).

If the person is a contact, follow the procedures for testing and evaluation in the Contact Investigation section of the manual (**9.1**).

If the person is a participant in two-step screening, refer to the topic entitled "Two-Step Tuberculin Skin Testing" in the Infection Control section of this manual of the manual (**11.13**).

If the TST result is positive, an interview and symptom check and a chest radiograph should be obtained for the patient.

Chest Radiography (X-ray)

All individuals being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease. For information on how to classify TB, see the "Tuberculosis Classification System" (**2.7**) in the Surveillance section of the manual. Refer to Table 4 which follows to determine when to obtain a chest radiograph and what follow-up is required for chest radiograph results.

A posterior-anterior radiograph of the chest is the standard view used for the detection and description of chest abnormalities in adults. In some instances, other views (e.g., lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.

Children younger than 5 years of age should have posterior-anterior and lateral radiographs performed. [25]

For more information on chest radiographs, refer to the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (Curry International Tuberculosis Center Web site; 2006) at http://www.currytbcenter.ucsf.edu/radiographic/ .

For persons recently exposed to TB, follow the procedures for testing and evaluation in the Contact Investigation section of the manual (**9.1**).

Pregnant women with a positive TST or IGRA should have a shielded chest radiograph. If the pregnant woman is asymptomatic and in the first trimester of pregnancy, the chest radiograph may be postponed until the second trimester[29].

TABLE 4: TARGETED TESTING FOR LATENT TUBERCULOSIS INFECTION: WHEN CHEST RADIOGRAPHS ARE REQUIRED AND HOW TO FOLLOW UP ON RADIOGRAPHY RESULTS

Signs or Symptoms of TB Disease?	TST or IGRA/QFT-G Result?	Recent Exposure to Infectious TB?	Chest Radiograph?	Follow-up Action
Yes	Positive or negative	Yes or no	Normal or abnormal	• Classify as Class 5. • Evaluate for TB disease.
No	Negative	No	CXR not recommended unless the patient has HIV infection or other forms of immunosuppression are present	• Classify as Class 0. Refer to the Diagnosis of Tuberculosis Disease section (4.1)
No	Positive	No	Normal	• Classify as Class 2. • Consider treatment for LTBI. Refer to the Treatment of Latent Tuberculosis Infection section (7.1)
			Abnormal: Noncalcified fibrotic lesions suggestive of old, healed TB; comparison film available and stable	• Classify as Class 4 or 5. • Consider evaluating for TB disease. Refer to the Diagnosis of Tuberculosis Disease section (4.1)
			Abnormal: Consistent with TB disease; no comparison film	• Classify as Class 3 or 5. • Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section (4.1)

Definitions of abbreviations: CXR = chest radiograph/x-ray; HIV = human immunodeficiency virus; IGRA = interferon gamma release assay/ QuantiFERON®-TB Gold (QFT-G); LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.

Resources and References

Resources

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[1] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54 (No. RR-12):15.

[2] CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9, 22.

[3] CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8–9.

[4] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54 (No. RR-15):52.

[5] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.

[6] CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4.

[7] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):52.

[8] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):50.

[9] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):52.

[10] CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):11; CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):13; County of Los Angeles Tuberculosis Control Program. *Tuberculosis Control Program Manual: 2003 Edition*:2-1. Available at: http://www.lapublichealth.org/tb/TBManual/TBmanual.pdf . Accessed January 10, 2012.

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DOH 343-071 June 2012
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Case Management

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- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Chart Audit Tool
- Civil Detention Flowchart
- Clinic Record (SHD)
- Contact Investigation
- Contact Investigation Instructions
- DOT Agreement (PHSKC)
- DOT Agreement (Virginia)
- DOT Audit Tool
- Drug Interview Sheet (SHD)
- Guidelines for Use of Videophone for DOT/DOPT (SHD)
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- Home Isolation Agreement (SHD)
- Interjurisdictional TB Notification
- Intake/Evaluation (Clark/Skamania Counties)
- Inventory and Tracking of Videophones
- Isolation Instructions (TPCHD)
- Isolation Instructions/Spanish (TPCHD)
- Job Description (SHD)
- Laboratory Data Sheet
- Medication Orders (SHD)
- Release of Liability
- Report of Loss, Theft, or Damage
- Requests for Loan of Videophone
- RVCT Form
- Personal Safety for Field Workers (Chelan/Douglas County)
- Protocol and Standing Orders (SHD)
- Public Health Directive (Adherence) (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)
- Screening Record (SHD)
- Sputum Collection (Chelan/Douglas County)
- TB Control Referral
- TB Flow Chart

Forms Used in this Section, Cont.

- Treatment Agreement (TPCHD)
- Treatment Agreement (Spanish) (TPCHD)
- Tuberculosis Drug Record
- Tuberculosis Screening Guidelines
- Videophone Direct Observed Therapy (TPCHD)
- Videophone Directly Observed Therapy Consent
- Videophone Directly Observed Therapy Memorandum
- Vision and Hearing Log (Virginia)

Quick Start Check List: Case Management

This check list is designed to assist public health nurses/TB case managers when managing a case. The tasks below should be performed by licensed nursing, medical, laboratory, and Disease Investigator staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Case Management	Instructions and Forms
When a suspected or confirmed case of tuberculosis (TB) disease is reported to the local public health agency: ☐ Receive the case report ☐ Assign the case manager ☐ Report electronically via PHIMS TB	Instructions: • Reporting Tuberculosis (**2.8**) • In the WAC, see Chapter 246-101 (Notifiable conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101 Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx • Protocol and Standing Orders (SHD) • Job Description (SHD) • Chart Audit
Take infection control precautions: Isolate the patient, if necessary (if the patient has positive acid-fast bacilli [AFB] sputum smear results and/or cavitary disease) or high suspicion for active TB even if smear negative Advise staff to take personal respiratory precautions, if necessary	**Instructions:** • Infection Control (**11.1**) **Forms:** • Personal Safety for Field Workers (Chelan/Douglas County) • Home Isolation Agreement (SHD) • Isolation Instructions (TPCHD) • Isolation Instructions (Spanish) (TPCHD) • Acknowledgement of TB Counseling (PHSKC) • Public Health Directive (Adherence) (PHSKC) • Public Health Directive (Non-Compliance) (PHSKC) • Authorization for Care Coordination (PHSKC) • Authorization for Disclosure of Protected Health Information (PHSKC) • Civil Detention Flowchart

Tasks for Case Management	Instructions and Forms
Perform the initial assessment of the patient: Start the initial assessment within ≤1 business day of the case report for infectious patients; and ≤3 business days of the case report for others. Consult with medical provider, local health officer, or DOH TB Medical Consultant within ≤1 business day of the case report Conduct an initial interview of the patient and visit the patient's home: • If the patient is hospitalized, conduct the initial assessment during the patient's hospitalization.* If the patient is not hospitalized, conduct the initial assessment at the first clinic visit or during a home visit • Collect and submit 3 sputum samples for AFB smear and culture (if not done earlier). Obtain specimens 8 to 24 hours apart with one being an early morning specimen • Visit the patient's home (if initial visit occurred in the hospital) within ≤3 business days of hospital discharge • Reinterview the patient within 1 to 2 weeks after the initial interview If the patient is hospitalized outside of his or her county of residence: The role of the LHJ TB Program in which patient is hospitalized is to coordinate with the LHJ TB Program of the patient's residence. Assure medical evaluation of the patient within 1 week of referral Submit the "Tuberculosis Contact Investigation Form" to WA State TB Services within 2 weeks Use the data collected from the physician consultation(s), record review, and patient interviews to complete the following tasks: • Review demographic information • Ascertain the extent of TB illness (See below for diagnosis of TB disease.) • Review the patient's health history • Determine the index patient's infectious period (count 3 months back from start of symptoms- cough, weight loss, fever, chest pain, night sweats) • Evaluate the patient's knowledge and beliefs about TB • Administer, measure, and interpret a Mantoux TST or IGRA • Screen for HIV • Obtain baseline biochemistry tests (CBC, Liver function) for toxicity monitoring (chose tests based on regimen and for special situations such as HIV infections, history of liver disease, alcoholism, and pregnancy):	**Instructions:** **Effective TB interviewing for Contact Investigation** Forms: • Home Evaluation (SHD) • RVCT Form • Intake/Evaluation (Clark/Skamania Counties) • Contact Investigation • Instructions

Tasks for Case Management	Instructions and Forms
• Complete blood count • Platelets • Liver function tests • Uric acid measurements Assure MD physical exam • Perform baseline visual acuity and color discrimination tests for toxicity monitoring if the patient is prescribed ethambutol • Initiating medical treatment (if not initiated during hospital stay) is recommended with a positive AFB sputum smear results • Monitor the TB medication regimen • Identify any barriers or obstacles to adherence • Review psychosocial status • Identify and document a complete history of patient's social network, to include home, social, work, and church site(s) • Initiate a contact investigation, if indicated • Assure that face-to-face initial encounters and skin testing or IGRA are conducted among high and medium priority contacts within 7 business days after their being listed in the investigation Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks • Assess patient for need to restrict travel (Do Not Board)	Instructions for Visual Acuity • http://www.toledo-bend.com/colorblind/Ishihara.asp Forms: • Contact Investigation • Instructions • Do Not Board Protocol
Assist in diagnosing TB disease: Assure that medical evaluations are conducted and treatment started for LTBI in high priority contacts who are children and/or have high-risk factors within 5 business days after initial encounters Assure that diagnostic tests and/or assessments are completed to diagnose TB disease or to rule out TB disease Receive initial AFB sputum smear tests (laboratory has to report within 2 days of AFB smear result) Assure NAA test is ordered, if needed to quickly confirm diagnosis of TB for a patient with positive AFB sputum smear. Results in 2-3 working days report of NAA Assure a medical evaluation of patient within 1 week of referral	**Instructions:** • Diagnosis of Tuberculosis Disease (**4.1**) • Bacteriology Tests (**4.19**) • Tuberculosis Screening Guidelines
Communicate to state TB Services staff: Submit to WA State TB Services via TB PHIMS within 7 days of the LHJ receiving notification of the suspect OR case Submit electronically TB PHIMS case reports from Level 1 sites; DOH receives these reports weekly on Friday	**Forms:** • RVCT Form

Tasks for Case Management	Instructions and Forms
Send to DOH via TB PHIMS when suspect becomes a case Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks	• Contact Investigation • Instructions
Assure that a treatment plan is developed and promptly initiated: Begin implementing the treatment plan: • Refer the patient to other healthcare providers, social service agencies, or community organizations as needed (case manager works as a liaison between the patient and other providers) • Broker and locate needed services relating to TB treatment • Negotiate a plan for directly observed therapy (DOT), Videophone DOT, or self-administration • Coordinate strategies to improve adherence If the patient is hospitalized, clarify the hospital discharge arrangements and assure that they are communicated to the hospital's outpatient coordinator and the treating physician(s) Identify and document drug treatment plan	**Instructions:** • Treatment (**5.10**) • Directly Observed Therapy (DOT)/Videophone (**8.51**) **Forms:** • Treatment Agreement (TPCHD) • Treatment Agreement (Spanish) (TPCHD) • DOT Agreement (Virginia) • DOT Agreement (PHSKC) • Tuberculosis Drug Record • Medication Orders (SHD)
Gather baseline data for toxicity monitoring: ☐ Obtain baseline biochemistry tests for toxicity monitoring (choose tests based on regimen and for special situations such as human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy): • Complete blood count • Platelets • Liver function tests • Perform baseline visual acuity and color discrimination tests for toxicity monitoring if the patient is prescribed ethambutol	**Instructions:** • Side effects and Adverse Reactions (**5.19**) The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Person Being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm **Forms:** • Treatment Agreement (TPCHD) • Treatment Agreement (Spanish) (TPCHD) • Laboratory Data Sheet Instructions For Visual Acuity http://www.toledo-bend.com/colorblind/Ishihara.asp
Provide DOT: Initiate DOT or Videophone DOT Assess adherence and drug toxicity at each visit Follow up missed appointments **on the same day**	**Instruction:** • Directly Observed Therapy (DOT)/Videophone (**8.51**) • Dot Audit Tool

Tasks for Case Management	Instructions and Forms
Monitor the patient regularly: Conduct ongoing assessment and monitoring at least monthly for clinical response, drug toxicity, and adherence Obtain and document HIV status. Refer patient for HIV treatment, if indicated Receive and review drug susceptibility results; results on first-line drugs should be available within 30 days from specimen receipt in the PHL. Review treatment. If there is concern regarding response or drug toxicity, consult with the medical provider, LHJ Health Officer, or DOH TB Services Medical Consultant 206- 718-2664. If a change directed, then document and implement the new medication orders Ensure that medications are ordered and are the correct dosage. If the patient is on isolation, determine when isolation can be discontinued If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported (this usually occurs within 2 months of treatment. If beyond 2 months then other tests are ordered.) Review the status of the contact investigation Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) • Available Laboratory Tests (**10.8**) • Drug Treatment (**5.10**) **Forms:** • Treatment Agreement (TPCHD) • Treatment Agreement (Spanish) (TPCHD) • RVCT Form • Contact Investigation • Instructions
Monitor the clinical response to treatment: Reassess information about the index patient weekly until drug susceptibility results are available or for 2 months after the case report, whichever is longer contact local health officer, medical provider, or WA State TB services medical consultant. Susceptibility reports are usually available within 28 days (first line of drugs) When the patient has negative AFB sputum smear results, then each month collect sputum specimens and submit them for testing until 2 consecutive negative culture results are reported • For multidrug-resistant TB (MDR-TB) patients, monthly specimens are required • For non-MDR-TB patients who can produce sputum, monthly specimens are recommended	**Forms:** • RVCT Form **Forms:** • Tuberculosis Screening Guidelines

Tasks for Case Management	Instructions and Forms
Monitor the clinical response to treatment (continued): ☐ Complete field investigation (visiting all potential transmission sites) within 5 days after starting the investigation ☐ Assess patient for need to restrict travel (do not board)	**Forms:** • Do Not Board Protocol
Monitor the patient for drug toxicity: Assess drug toxicity at each DOT visit Repeat liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) when the patient is taking isoniazid, a rifamycin, or pyrazinamide if • Baseline results are abnormal • The patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • The patient has symptoms of adverse reactions If the patient is taking ethambutol, evaluate the patient monthly regarding possible visual disturbances, including blurred vision or scotomata Test visual acuity and color discrimination monthly when the patient is taking ethambutol	**Instructions:** • Side effects and Adverse Reactions (**5.19**) Instructions For Visual Acuity • http://www.toledo-bend.com/colorblind/Ishihara.asp
Assess adherence and address obstacles to adherence: Assess adherence weekly and monthly and identify positive and negative motivational factors influencing adherence Determine the unmet educational needs of the patient Educate the patient about the TB disease process Advocate for the patient with team members and other service providers Each week, review documentation to ensure that the contact list is complete Assure that contacts are assessed monthly for: • Clinical follow-up • Adherence to LTBI treatment • Adverse reactions to LTBI treatment On contacts whose results were initially negative, repeat TST or IGRA 8-10 weeks after contacts last exposure to the index patient during the infectious period Address nonadherence, if necessary: • Review with the patient the treatment agreements and directly observed therapy arrangements	**Forms:** • Treatment Agreement (TPCHD) • Treatment Agreement (Spanish) (TPCHD) • DOT Agreement (Virginia) • DOT Agreement (PHSKC)

Tasks for Case Management	Instructions and Forms
Assess adherence and address obstacles to adherence (continued): • Educate the patient about TB and its treatment • Refer the patient to social services, if necessary • Provide incentives and enablers Initiate legal orders, if other measures do not improve adherence	**Instructions:** **Due Process** • WAC 246-170-051 • WAC 246-170-055
Confirm the completion of treatment: Verify completion of treatment after treatment was started based on: • Regimen • Interruptions • Response to treatment • Number of weeks on DOT • Number of doses taken (weekly and twice, thrice, and once weekly) Submit to DOH via PHIMS TB	**Forms:** • RVCT Form • DOT Agreement (Virginia) • DOT Agreement (PHSKC)
Evaluate case management activities: Monitor the activities against the treatment plan monthly (or more frequently if needed) Document as activity occurs and at least monthly on the LHJ patient record	**Forms:** • Clinic Record (SHD) • Sputum Collection (Chelan/Douglas County)

To understand the evaluation process in diagnosing TB disease and LTBI, view the "Tuberculosis Screening Guidelines" provided on page **4.6.**

Suggested use of Time Frames and Task Assignments for diagnosis, treatment, and contact investigation of a patient with TB (Roadmap): Use this table as a quick reference list of tasks or use it as a check list for to track that tasks are completed for a specific patient. To read this table, start at the top row and read it from left to right. Continue to the next row below and read it from left to right. Note that this table shows the general sequence of tasks, and the sequence of tasks may differ for individual patients. Also note that not all tasks may be required for all patients. To use this table as a check list, place a copy in the patient's chart and initial in the box next to each task when it is completed. If a task is not needed, cross it off the table. Initial at the bottom of each page when the page is completed.

TABLE 2: TIME FRAMES & TASK ASSIGNMENTS FOR DIAGNOSIS, TREATMENT, AND CONTACT INVESTIGATION OF A PATIENT WITH TB

MONTH 1 - Week 1*				
Start of initial assessment	Receive the TB suspect/case report and notify the WA State DOH[___]	Assign the case manager [___] ▪ Advise staff to take personal respiratory precautions, if necessary	Isolate the patient, if necessary (if the patient has positive AFB sputum smear results and/or cavitary disease) [___]	Start the initial assessment within ≤1 business day of notification of the case [___]
Initial interviews and consultations	Consult with the responsible physician and/or program medical consultant for medical examination/case review **within ≤1 day of notification of the case** [___]	Interview the patient **within ≤1 business day of the case report** (begin patient education, collect patient data to determine infectious period, and gather contact investigation data if needed) [___] ▪ Home evaluation ▪ RVCT Form/TB contact report		Visit the patient's residence **within ≤3 business days after first interview** (collect contact investigation data if needed) [___] ▪ Reinterview 1-2 weeks
Medical evaluation	Assure a medical evaluation of the patient **within 1 week of referral** [___] Refer to Protocol and Standing Orders	Screen for HIV [___]	Administer, measure, and interpret a Mantoux TST (or IGRA) [___]	Collect and submit 3 sputum specimens for AFB smear and culture (if not done earlier). Obtain specimens 8 to 24 hours apart with one being an early morning specimen [___]
	Gather medical history [___]	Conduct a physical examination [___]	Order chest radiography [___]	
After AFB sputum smear testing completed	Receive results of AFB sputum smear tests (laboratory has to report within 2 days of AFB smear result) [___] In the WAC, see chapter 246-101 (Notifiable Conditions)	Assure that an NAA (MTD) test is ordered, if needed to quickly confirm diagnosis of TB for a patient with positive AFB sputum smear. Results in 2-3 working days report of MTD [___]	Send the written "Confirmed/Suspected Report of Tuberculosis Disease" to the Washington TB Program **within 7 days LHJ receiving notification of suspect or confirmed case** [___]	Determine the index patient's infectious period (count three months back from start of symptoms-cough, weight loss, fever, chest pain, night sweats) [___]
After sufficient medical and laboratory assessment data gathered	For a hospitalized patient, clarify the hospital discharge arrangements and assure that they are communicated to the hospital's outpatient coordinator and the treating physician(s) [___]	Obtain baseline biochemistry tests† for toxicity monitoring (choose tests based on regimen and for special situations such as HIV infection, history of liver disease, alcoholism, and pregnancy): ▪ Complete blood count ▪ Platelets	Perform baseline visual acuity and color discrimination tests† for toxicity monitoring if the patient is prescribed ethambutol[___]	Begin implementing the treatment plan [___] Refer to Protocol and Standing Orders
			Assure that a written treatment plan is developed [___]	Initiating medical treatment is recommended with a

		▪ Liver function tests ▪ Uric acid measurements [___]	Assure that education is provided to the patient and provider as needed when their signatures are obtained on the treatment plan [___]	positive AFB sputum smear results [___]
Decision to conduct an investigation	Gather the index patient's medical records (from hospital, clinic, and/or healthcare provider) (See patient interview and home visit above in the Initial Interviews row.) [___]		Decide if a contact investigation is indicated (based on positive AFB sputum smear results and/or cavitary disease or pleural TB) [___]	If an investigation is indicated, start the contact investigation **within ≤1 business day of notification of the suspect or confirmed case** [___]
Contact list	During the index patient interview, start listing names and locating information of named contacts and continue listing them throughout the investigation [___]		Assign an initial priority classification to each contact (and revise as needed when new information is received) [___]	Review all documentation to ensure that the contact list is complete [___] ▪ Report contacts to DOH TB Services within 2 weeks

* When a task needs to be completed before the end of the first week, its time frame is bolded.
† For more information on baseline testing, refer to Table 8 in the Treatment of TB Disease section.

MONTH 1 - Week 2*				
Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___]	If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported (this usually occurs within 2 months of treatment. If beyond 2 months then other tests are ordered.) [___]	Reassess information about the index patient weekly until drug susceptibility results are available or for 2 months after the case report, whichever is longer Susceptibility reports are usually available within 28 days (first line drugs) if drug resistance then it may take 30 or more additional days to determine total drug resistance. [___]	If the patient is isolated, determine whether isolation can be discontinued based on conversion of negative sputum smear and culture and if patient is sensitive to all first line drugs. [___]
	Follow up missed appointments on the same day [___]	If the patient initially had positive AFB sputum smear results quantified as 3+ to 4+ and/or cavitation, continue collecting one specimen each week until 3 consecutive negative smears and negative culture [___]	Reassess treatment, side effects, and adherence and, if concerned, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs[___] Refer to Protocol and Standing Orders	

Field investigation and interviews	Complete the field investigation (visiting all potential transmission sites) **within 5 days after starting the investigation** [___]	Reinterview the index patient in their home **within 2 weeks after the first interview** [___]		
Contact evaluation	Assure that face-to-face initial encounters and skin testing or IGRAs are conducted among high- and medium-priority contacts **within 7 business days after their being listed in the investigation** [___]	Assure that medical evaluations† are conducted and treatment started for LTBI in high-priority contacts who are children and/or have high-risk factors **within 5 business days after initial encounters** [___]	Assure that medical evaluations† are conducted of other high-priority contacts to index patients with positive AFB sputum smear results **within 5 business days after initial encounters** [___]	Review and assess the completeness of contacts' medical follow-up and treatment plans **within 5 business days after their medical evaluations** [___]
Data review and reporting	Each week, review documentation to ensure that the contact list is complete [___]	Each week, collect and analyze data on contacts and TSTs or IGRAs; reassesses contact priorities [___]	Decide whether to continue/expand the investigation based on analysis of TST or IGRA data [___]	Report to the Washington TB Program **after initial tuberculin skin testing or IGRA is completed** [___]

* Most tasks listed on this page should be started and completed during the second week. When a task's time frame may fall outside of the second week, its time frame is bolded.
† Medical evaluation for TST- or IGRA positive contacts includes history and chest radiography. For contacts with symptoms of TB disease, evaluate with history and bacteriology tests.

MONTH 1 - Weeks 3 and 4*

Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___] Follow up missed appointments on the same day [___]	If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported [___]	Reassess information about the index patient weekly **until drug susceptibility results are available and then reassess at least monthly** [___] Reassess treatment, side effects, and adherence and, if concerned, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs[___] Refer to Protocol and Standing Orders	If the patient is isolated, determine whether isolation can be discontinued based resolution of symptoms and current treatment and 3 negative smears and negative cultures and patient is on current treatment with antituberculosis regimen to which strain is known to be susceptible. [___]
Contact evaluation and treatment	Assure that face-to-face initial encounters and skin (or IGRA) testing are conducted among high- and medium-priority contacts **within 3**	Assure that medical evaluations† are conducted and treatment started for LTBI in high-priority contacts who are children and/or have high-risk factors	Assure that medical evaluations† are conducted of other high-priority contacts to index patients with positive AFB sputum smear results **within 5**	Assure that medical evaluations† are conducted of high-priority contacts to AFB-sputum- smear-negative index patients and medium-priority contacts

	business days after their being listed in the investigation [___]	**within 5 business days after initial encounters** [___]	**business days after initial encounters** [___]	**within 10 business days after initial encounters** [___]
	Assure that treatment is started for LTBI in adult high- and medium-priority contacts without high-risk factors **within 10 business days of their medical evaluations** [___]	Review and assess the completeness of contacts' medical follow-up and treatment plans **within 5 business days after their medical evaluations** [___]	Review and assess the timeliness of initiating the treatment plans for contacts **within 10 business days after their medical evaluations** [___]	
Data review and reporting	Each week, review documentation to ensure that the contact list is complete [___]	Each week, collect and analyze data on contacts and TSTs or IGRAs; reassesses contact priorities [___]	Decide whether to continue/expand the investigation based on analysis of TST or (IGRA) data [___]	Report to the Washington State DOH TB Program **after initial tuberculin skin testing is completed** [___]

* Most tasks listed on this page should be started and completed during the third and fourth weeks. When a task's time frame may fall outside of the third and fourth weeks, its time frame is bolded.
† Medical evaluation for TST- or IGRA positive contacts includes history and chest radiography. For contacts with symptoms of TB disease, evaluate with history and bacteriology tests.

MONTH 2*				
Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___]	Conduct ongoing assessment and monitoring at least monthly (clinical response, adverse reactions, adherence) [___]	If the patient has negative AFB sputum smear results, each month collect sputum specimens and submit them for testing until 2 consecutive negative culture results are reported [___]	If sputum smear results are positive **after 2 months of treatment**, call the local health officer, medical provider, or Washington State Medical Consultant 206-718-2664 [___] Refer to Protocol and Standing Orders
	Follow up missed appointments on the same day [___]	If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported [___]	Call the local health officer, medical provider, or Washington State Medical Consultant to determine how to monitor when the patient ▪ Is culture negative ▪ Had AFB 3+ or 4+ results and/or cavitation on x-ray or ▪ Had no sputum specimens collected [___]	

	Repeat liver function tests (AST, ALT, and serum bilirubin)† when the patient is taking isoniazid, a rifamycin, or pyrazinamide if ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions [___]	Question the patient taking ethambutol monthly regarding possible visual disturbances, including blurred vision or scotomata [___] Test visual acuity and color discrimination monthly when the patient is taking ethambutol† ▪ In doses >15–25 mg/kg ▪ For >2 months ▪ With renal insufficiency [___]	Receive culture results [___] Reassess information about the index patient weekly **until drug susceptibility results are available or for 2 months after the case report, whichever is longer** [___] Reassess treatment, side effects, and adherence and, if concerned, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs[___]	If the patient is isolated, determine whether isolation can be discontinued [___] Send updates with changes in treatment plan to Washington State DOH TB Services [___]
Contact evaluation and treatment	Assure that contacts are assessed monthly for ▪ Clinical follow-up ▪ Adherence to LTBI treatment ▪ Adverse reactions to LTBI treatment [___]	On contacts whose results were initially negative, repeat TST or IGRA testing 8 to 10 weeks after each contact's last exposure to the index patient during the infectious period [___]	**After retesting**, reevaluate contacts who were initially TST- or IGRA negative and started on LTBI treatment to determine if treatment should be continued [___]	
Data review and reporting	Each week, review documentation to ensure that the contact list is complete [___]	Each week, collect and analyze data on contacts and TSTs or IGRAs; reassess contact priorities [___]	Determine if transmission occurred and whether to expand the investigation [___]	Send contact information to Washington State DOH TB Services **after retests are completed** [___]

* Most tasks listed on this page should be started and completed during the second month. When a task's time frame may fall outside of the second month, its time frame is bolded.
† For more information on follow-up testing, refer to Table 8 in the Treatment of TB Disease section.

MONTHS 3 through 5*

Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___]	Conduct ongoing assessment and monitoring at least monthly (clinical response, adverse reactions, adherence) [___]	When the patient has negative AFB sputum smear results, each month collect sputum specimens and submit them for testing until 2 consecutive negative culture results are reported [___]	If sputum smear results or culture results are positive **after 2 months of treatment**, call the medical provider, local health officer, or Washington

	Follow up missed appointments on the same day [___]	If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, each week collect sputum specimens and submit them for testing until 3 consecutive negative AFB sputum smear results are reported[___]	Call the local health officer or Washington State Department of Health Medical Consultant to determine how to monitor when the patient ▪ Is culture negative ▪ Had AFB 3+ or 4+ results and/or cavitation on x-ray or ▪ Had no sputum specimens collected [___]	State Medical consultant (206) 718-2664 [___]
	Repeat liver function tests (AST, ALT, and serum bilirubin)† when the patient is taking isoniazid, a rifamycin, or pyrazinamide if ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions [___]	Question the patient taking ethambutol monthly regarding possible visual disturbances, including blurred vision or scotomata [___] Test visual acuity and color discrimination monthly when the patient is taking ethambutol† ▪ In doses >15–25 mg/kg ▪ For >2 months ▪ With renal insufficiency [___]	Reassess treatment, side effects, and adherence and, if concerned, consult with the medical provider, local health officer, or Washington State Medical consultant 206-718-2664. If a change is decided upon, obtain new physician's orders and order drugs [___] Refer to Protocol and Standing Orders	Send updates with changes to the treatment plan to Washington State DOH TB Services [___]
Contact treatment and investigation	Assure that contacts are assessed monthly for ▪ Clinical follow-up ▪ Adherence to LTBI treatment ▪ Adverse reactions to LTBI treatment [___]	Each week, review documentation to ensure that the contact list is complete [___]		

* Most tasks listed on this page should be started and completed during the third to fifth months. When a task's time frame may fall outside of this period, its time frame is bolded.
† For more information on follow-up testing, refer to Table 8 in the Treatment of TB Disease section.

MONTHS 6 through 9*

Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___]	Follow up missed appointments on the same day [___]	Conduct ongoing assessment and monitoring at least monthly (clinical response, adverse reactions, adherence) [___]	When the patient has negative AFB sputum smear results, each month collect sputum specimens and submit them for testing until 3 consecutive negative culture results are reported [___]

	Repeat liver function tests (AST, ALT, and serum bilirubin)† when the patient is taking isoniazid, a rifamycin, or pyrazinamide if ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions [___]	Question the patient taking ethambutol monthly regarding possible visual disturbances, including blurred vision or scotomata [___] Test visual acuity and color discrimination monthly when the patient is taking ethambutol† ▪ In doses >15–25 mg/kg ▪ For >2 months ▪ With renal insufficiency [___]	Reassess treatment, side effects, and adherence and, if concerned, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs[___] Refer to Protocol and Standing Orders Verify completion of treatment **6 to 9 months after treatment was started** (depending upon regimen, adherence, response to treatment, number of weeks on DOT, and number of doses taken) [___]	Send updates for completion of therapy to Washington State DOH TB Services [___]
Contact treatment and investigation	Assure that contacts are assessed monthly for ▪ Clinical follow-up ▪ Adherence to LTBI treatment ▪ Adverse reactions to LTBI treatment [___]	Verify completion of treatment **6 to 9 months after treatment was started** (depending upon regimen, adherence, number of weeks on treatment and/or number of doses taken) [___]	Each week, review documentation to ensure that the contact list is complete [___]	

* Most tasks listed on this page should be started and completed during the sixth to ninth months. When a task's time frame may fall outside of this period, its time frame is bolded.
† For more information on follow-up testing, refer to Table 8 in the Treatment of TB Disease section.

MONTHS 10 through 12*

Case management of index patient	Provide directly observed therapy and assess adherence and side effects/adverse reactions at each visit [___]	Follow up missed appointments on the same day [___]	Conduct ongoing assessment and monitoring at least monthly (clinical response, adverse reactions, adherence) [___]	When the patient has negative AFB sputum smear results, each month collect sputum specimens and submit them for testing until 3 consecutive negative culture results are reported [___]

	Repeat liver function tests (AST, ALT, and serum bilirubin)† when the patient is taking isoniazid, a rifamycin, or pyrazinamide if ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions [___]	Question the patient taking ethambutol monthly regarding possible visual disturbances, including blurred vision or scotomata [___]	Reassess treatment, side effects, and adherence and, if concerned, consult with the treating physician. If a change is decided upon, obtain new physician's orders and order drugs[___] Refer to Protocol and Standing Orders	Send updates for completion of therapy to Washington State DOH TB Services [___]
		Test visual acuity and color discrimination monthly when the patient is taking ethambutol† ▪ In doses >15–25 mg/kg ▪ For >2 months ▪ With renal insufficiency [___]	Verify completion of treatment **if treatment time was prolonged** (depending upon regimen, adherence, response to treatment, number of weeks on DOT, and number of doses taken) [___]	
Contact treatment and investigation	Assure that contacts are assessed monthly for ▪ Clinical follow-up ▪ Adherence to LTBI treatment ▪ Adverse reactions to LTBI treatment [___]	Verify completion of treatment **9 to 12 months after treatment was started** (depending upon regimen, adherence, number of weeks on treatment and/or number of doses taken) [___]	Each week, review documentation to ensure that the contact list is complete [___]	Report to the Washington State DOH TB Program **after contacts complete treatment for LTBI** [___]
			Collect and analyze data [___]	Collect data to complete the *ARPE* form [___]

* Most tasks listed on this page should be started and completed during the tenth to twelfth months. When a task's time frame may fall outside of this period, its time frame is bolded.
† For more information on follow-up testing, refer to Table 8 in the Treatment of TB Disease section.

Introduction

Purpose

Tuberculosis (TB) case management describes the activities undertaken by the local health jurisdiction (LHJ) and its partners to ensure successful completion of TB treatment and cure of the patient.[1] Case management is a system in which a specific health department employee is assigned primary responsibility for the patient, systematic regular review of patient progress is conducted, and plans are made to address any barriers to adherence.[2]

Use this section to understand and follow national and Washington State guidance to do the following:

- Conduct initial assessments
- Develop treatment plans for case management activities
- Conduct monthly ongoing assessments
- Monitor adverse reactions to antituberculosis medications and monitor toxicity
- Monitor bacteriologic and clinical improvement
- Verify completion of therapy
- Evaluate case management activities
- Understand Cohort Review
- Provide directly observed therapy (DOT) and videophone DOT
- Use incentives and enablers to improve adherence to therapy
- Understand when and how to use legal orders, if necessary, for adherence to therapy

One of the four fundamental strategies to achieve the goal of TB control in the United States is the early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment. Completion of a full course of standard therapy is essential to prevent treatment failure, relapse, and the development of drug resistance.[3]

One reason for failure to complete standard treatment is that patients frequently fail to adhere to the lengthy course of treatment. Poor adherence to treatment regimens might result from difficulties with access to the healthcare system, cultural factors, homelessness, substance abuse, lack of social support, rapid clearing of symptoms, or forgetfulness.[4]

These adverse outcomes are preventable by case-management strategies provided by TB control programs, including use of DOT and videophone DOT.[5] It is strongly recommended that the initial treatment strategy utilize patient-centered case management with an adherence plan that emphasizes DOT.[6] It is essential to provide patient-centered case management in which treatment is tailored and supervision is based on each patient's clinical and social circumstances.[7] Programs utilizing DOT as the central element in a comprehensive, patient-centered approach to case management (enhanced DOT) have higher rates of treatment completion than less intensive strategies.[8]

Policy

Although some patients may undergo most of their evaluation and treatment in settings other than a local public jurisdictions, LHJs should undertake the major responsibility for monitoring and ensuring the quality of all TB-related activities in the community as part of its duties to protect the public health.

Effective TB case management requires administrative commitment and support. This includes education, staff training, and ensuring adequate funding to maintain program activities. It is recognized that LHJs differ in their staffing and organization and that no set of guidelines can cover all the situations that may arise relating to case management.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction (**1.16**).

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

Forms

To identify required and recommended forms, refer to the "Quick Start Check List: Case Management" in this section (**8.4**).

Acknowledgments

The authors want to acknowledge the extensive use of two non–Centers for Disease Control and Prevention (CDC) sources for the content in this section.

The New Jersey Medical School National Tuberculosis Center's *Tuberculosis Case Management for Nurses: Self-Study Modules* course is a comprehensive and well-written overview of case management for a national audience. The text for large portions of the "Initial Assessment," "Treatment Plan," and "Ongoing Assessment and Monitoring" topics was taken and/or adapted from the second module of this self-study course.

The California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA) "TB Case Management—Core Components" guideline provides another comprehensive source of recommendations on case management practices. This guideline is one in the series of *CDHS/CTCA Joint Guidelines* and is used throughout urban and rural areas in California. Some content in the "Ongoing Assessment and Monitoring" topic was taken from the "TB Case Management—Core Components" guideline.

Initial Assessment

Conduct initial assessments of tuberculosis (TB) patients to gather data that will form the basis for TB treatment and care. It is essential to gather data to determine the clinical and social issues and circumstances of relevance to the patient and to assess each situation objectively to determine the appropriateness of the planned intervention. Many professionals involved in the patient's care contribute to the assessment data, and the case manager gathers assessment data from many sources, including community agencies, medical providers, schools, and other healthcare facilities.[9]

When the patient with TB is a child, the case manager should involve both the child and family in the assessment process.[10]

To report TB cases (both suspected and confirmed), use PHIMS TB.

Cultural Sensitivity and Language Issues

In the initial assessment, consider cultural sensitivity and language issues. To improve the validity and quality of the assessment information, healthcare workers need to be culturally sensitive in approaching each patient. A medical interpreter may be needed for patients whose primary language is not English.

For more information on cultural sensitivity, refer to the *Participant's Workbook* for Session 4: "Working with Culturally Diverse Populations" in *DOT Essentials: The DOT Trainer's Curriculum* (Curry International Tuberculosis Center Web site; 2003) at http://www.currytbcenter.ucsf.edu/catalogue/epub/index.cfm?tableName=DOTE

For assistance with language issues, see the National Health Law Program and The National Council on Interpreting Health Care's *Language Services Resource Guide for Health Care Providers* (National Health Law Program Web site; October 2006) at http://www.healthlaw.org/images/stories/issues/ResourceGuideFinal.pdf .

Minnesota Department of Health's (MDH) Refugee Health and Tuberculosis Programs are pleased to offer a show about tuberculosis (TB) for the public, which can be found at http://www.health.state.mn.us/divs/idepc/diseases/tb/echo.html

Another resource for information about cultural beliefs, medical issues and other related issues pertinent to health case can be found at http://www.ethnomed.org/

For more information on using interpreters, see the *Interpretation Services* lesson in Module 9: "Patient Adherence to Tuberculosis Treatment" of the CDC's *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999) at http://www.cdc.gov/tb/education/ssmodules/module9/ss9contents.htm .

The Georgia Department of Health website has treatment consent forms for LTBI, active disease, DOT etc in a variety of languages at http://health.state.ga.us/programs/tb/phclinicforms.asp.

Patient's Medical Records

The case manager needs all medical records in order to provide case management and recommend a case management plan. Prior to the visit with the patient, the case manager should ensure that a copy of all of the patient's medical records (from hospitals, clinics, and other healthcare providers) and chest radiographs are available to the treating physician. Without the medical records, the physician may not be able to make the correct judgments in medical management.[11]

Assessment Site

If the patient is hospitalized, conduct the initial assessment during the patient's hospitalization. If the patient is hospitalized outside of his or her county of residence, coordinate with the other county or hospital's infection control staff to conduct the assessment. If the patient is not hospitalized, conduct the initial assessment at the first clinic visit or during a home visit. Start the initial assessment within 1 business day of the case report for infectious or smear positive pulmonary cases; and ≤3 business days of the case report for others. See MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis.

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm.

Discharge Planning

Patients who are diagnosed with TB during a hospitalization will require discharge planning. The case managers should ensure that appropriate discharge planning occurs for all patients with TB, to prevent transmission in the community and interruption in treatment.[12]

Initial Assessment Activities

To complete an initial assessment, perform the following activities:

Visit the patient's home within ≤3 days of the initial interview. See "Field Investigation", p. 8, MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

- Obtain or review demographic information
- Ascertain the extent of TB illness
- Obtain and review the patient's health history

Determine infectiousness or potential infectiousness, and window of infectiousness, if patient is sputum smear positive or has cavitation on CXR; see MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, specifically Factors for Assigning Contact Priorities, p. 10 and Figures 2-4 on pgs 12-14.
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

Evaluate the patient's knowledge and beliefs about TB

- Initiate treatment, if not initiated during the hospital stay
- Monitor the TB medication regimen
- Identify any barriers or obstacles to adherence
- Review psychosocial status
- Identify and document a complete history of the patient's social network, to include home, social, work, and church site(s)
- Initiate a contact investigation, if indicated

Visit the patient's home. During the patient's TB treatment, at least one or more home visits are required. Home visits are useful for confirming the patient's address, particularly for patients at high risk for default from treatment. Information gathered at the patient's home is often more revealing than assessments performed in the hospital, clinical or health department settings and can lead to a more accurate understanding of the patient's lifestyle (for example, seeing a child's shoes or toys when a child was not named in the contact investigation).[13] Several home visits may be needed, because usually not all of the necessary information is gathered from the patient and his or her family at one time.

After patient interview and identification of patient's social network, then initiate visit to employment sites. Site visits are complementary to interviewing. Contacts from these sites are often the most reliable source of information regarding transmission. See MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, specifically "Congregate Settings" p. 26) http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

Obtain or review demographic information, including the name, address, telephone number(s), birth date, and health insurance provider's name, address, and identifying information.[14]

Ascertain the extent of TB illness, including acuity and length of symptoms (for window of infectiousness), bacteriologic and radiographic findings, laboratory analyses, tuberculin skin test results, nutritional status, vital signs, and baseline weight (without shoes or excess clothing). Assess temperature, pulse, and respiration if the patient appears ill or the history suggests illness. Blood pressure evaluations are valuable, especially if the patient has no primary care provider and needs a referral to one.

The Local Health Officer should be consulted immediately upon receipt of a suspect report. Within one week of a case report, a tuberculin skin test should be placed, measured, and interpreted or IGRA; and a chest radiograph should be taken and interpreted. Also within one week of a case report, a minimum of three consecutive sputum specimens of good quality should be collected 8–24 hours apart (with at least one being an early morning specimen) and submitted to the laboratory.

In the case of pulmonary TB in children younger than 5 years of age, posterior-anterior and lateral chest radiographs are important in the initial diagnosis.[15] Adults who are suspected of TB or who are active cases usually need only an initial posterior-anterior and lateral chest radiograph.

Obtain and review the patient's health history to determine concurrent medical problems, including human immunodeficiency virus (HIV) disease or risk factors, country of birth, sexual history and partners, allergies, or medications that may interfere with TB drugs. The case manager should obtain the names, addresses, and telephone numbers of the patient's medical provider and any specialists involved in his or her medical care, previous hospitalizations, allergies, and current medications. It is important to know the history of treatment for TB infection and/or disease, especially for patients who are treatment failures or have a relapse of TB disease, as they are at a higher risk for developing multidrug-resistant TB (MDR-TB). It is also important to determine what the patient perceives as his or her most important medical/health problem(s). The date of the last menstrual period and contraceptive use should be obtained from female patients.[16]

Some antituberculosis medications are contraindicated when a patient is taking birth control pills. For more information, see the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section of the manual (**5.19**).

PRIORITY: Determine infectiousness or potential infectiousness. "Infectious" refers either to TB disease of the lungs or throat, which has the potential to cause transmission to other persons, or to the patient who has TB disease.

This focuses the contact investigation on those contacts most likely to be at risk for infection and sets the timeframe for testing contacts. This assessment should include the duration and frequency of symptoms, especially cough, and a review of the radiographic findings. If the patient is infectious or potentially infectious, the case manager should have an understanding of the period of infectiousness (window of infectiousness). The parameters of a contact investigation, including the need for repeating the tuberculin skin test or IGRA tests, test for contacts that were initially negative, can then be determined.[17]

A source-case investigation seeks the source of recent *Mycobacterium tuberculosis* infection, perhaps newly diagnosed TB disease. TB disease in children younger than 5 years typically indicates that the infection is recent. The yield of source-case investigations for children who have TB disease varies, typically less than 50%. A younger age cut-off might be advisable, because the focus would be on more recent transmission. If a source case is identified, dates of exposure and most recent information concerning the infectiousness of the source should be documented.

For more information on the period of infectiousness and contact investigations, see “Infectious Period” in the Contact Investigation section of the manual (**9.22**).

Evaluate the patient’s knowledge and beliefs about TB, including a history of TB in family and/or friends and the response to treatment. The case manager can assess TB knowledge by interviewing the patient regarding TB transmission, pathogenesis, and symptoms. Patient education should be based on current knowledge and ability to comprehend written, visual, and/or verbal information.[18]

It is important to interview both the child and parent or guardian in their own language when assessing TB knowledge; however, adolescents should be given the opportunity to speak to a healthcare provider alone. Keep in mind that parents who have misinformation or cultural bias about TB may affect their children’s understanding of the disease.[19] Use age-appropriate educational materials and methods, especially when working with children. When working with a school-aged child, it is important to explain that TB is treatable; and with the adolescent, it may be necessary to constantly reaffirm confidentiality.[20]

Initiate treatment. Initiation of treatment with a four-drug regimen should be initiated promptly when a patient is seriously ill (history of cough, hemoptysis, night sweats, fever, weight loss, chest pain, abnormal radiographs, sputum smear positive) with a disorder that is thought possibly to be tuberculosis. Initiation of treatment should not be delayed because of negative AFB smears for patients in whom tuberculosis is suspected and who have a life-threatening condition. Disseminated (miliary) tuberculosis, for example is often associated with negative sputum AFB smears. Likewise, for a patient with suspected tuberculosis and a high risk of transmitting *M. tuberculosis* if, in fact, she or he had the disease, combination chemotherapy should be initiated in advance of microbiological confirmation of the diagnosis to minimize potential transmission (see MMWR Treatment of Tuberculosis, 2003, specifically "Deciding to Initiate Treatment", p. 40 at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf).

The case manager should order drugs immediately upon receipt of medical orders which document drugs, dose, route, frequency, and duration.

Monitor the TB medication regimen. The case manager should ensure that medications and dosages are prescribed according to the current guidelines of American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC)/Infectious Diseases Society of America (IDSA). If the initial assessment occurs during the patient's hospitalization, the case manager should ensure that the ingestion of the TB medication is observed by a nurse. It is important to ensure that hospitals order and give dosages according to current ATS/ CDC/IDSA guidelines and are observing patients taking medications. Since the outpatient phase of treatment will involve giving all TB medications at one time, hospitals should be discouraged from splitting dosages for two reasons: (1) taking medications more than once a day creates an expectation for the patient that will have to change after discharge from the hospital, and (2) tolerance to the full dosage cannot be assessed while in the hospital. The patient's tolerance to TB medications should be noted. Additionally, possible interactions with other medications should be determined prior to the patient starting TB medications.[21]

For more information on "Treatment regimens and dosages" see the Treatment of Tuberculosis Disease section of the manual (**5.10**).

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

Identify any barriers or obstacles to adherence in taking TB medications and keeping physician or clinic appointments. This includes such issues as language, availability of transportation, the patient's preference for place and time of directly observed therapy (DOT), and the ability to swallow pills. Many adolescents and adults who have difficulty swallowing pills are embarrassed to report this to the healthcare provider. It may be necessary to teach people how to take pills, or it may be necessary to crush the pills and put them in food, such as pudding or applesauce. In addition, the case manager should determine the need for enablers and identify incentives that will be most valuable to the patient.[22] See "Incentives and Enablers" in this section of the manual (**8.59**).

Review psychosocial status to identify unmet needs, the use of alcohol and/or illegal drugs, and any pre-existing psychiatric diagnoses.[23]

Identify and document a thorough history of the patient's social network. This is important to identify and document in the event that the patient does not return for follow-up. The case manager needs to verify the patient/family's address, evaluate residential stability, and assess potential for homelessness. Determine the patient's residence(s) during the past year, particularly any congregate living situations, such as prison, jail, homeless shelter, nursing home, boarding home, or foster care. Establish the patient's occupation and/or student status, and document the name and address of business or school. The name and location of a child's babysitter, other caretakers, daycare center, and/or school should be noted. In order to identify those who have shared common air space with the infectious, untreated patient with TB, it is necessary to have an understanding of the patient's social and recreational activities and how he/she spends leisure time. This includes time spent at bars, floating card games, circuit parties, faith-based functions, and other social venues.

Gather information for a possible contact investigation.

For more information, see "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Treatment Plan

When sufficient information has been gathered by members of the healthcare team to assess a patient's needs and problems, the case manager should develop a treatment plan for each patient with confirmed or suspected tuberculosis (TB). The plan should combine both medical management of the patient and nursing interventions. Due to the length of TB treatment (from 6 to 24 months or longer), the plan must include intermediate and expected outcomes.

To ensure that therapy is completed, a treatment plan should be based on data collected by the healthcare team and must be designed to meet the patient's medical and personal needs. Treatment of a patient with TB is most successful within a comprehensive framework that addresses both clinical and social issues of relevance to the patient. **Patient-centered care is essential to provide** because it tailors treatment and bases supervision on each patient's clinical and social circumstances.

Each patient's management plan should be individualized to incorporate measures that facilitate adherence to the drug regimen, such as social service support, treatment incentives and enablers, housing assistance, referral for treatment of substance abuse, and coordination of TB services with those of other providers.[24]

In the initial management strategy, regardless of the source of supervision, always include an adherence plan that emphasizes directly observed therapy (DOT), in which patients are observed as they ingest each dose of antituberculosis medications, to maximize the likelihood of completion of therapy.[25]

The case manager is responsible for the overall plan, including documentation, monitoring the patient response, interventions, intermediate and expected outcomes, and initiating changes in the plan to reflect changes in circumstances.[26] The treatment plan should be reviewed and updated at least monthly during reviews of clinical progress.[27]

See other forms listed:

- Acknowledgement of Counseling (PHSKC)
- Public Health Directive (Adherence) (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)
- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Protocols and Standing Orders (SHD)
- Civil Detention Flowchart

Treatment Plan Components

Recommended components of a treatment plan include the following:

- Patient's verified address and contact information
- Assignment of responsibilities: case manager, clinical supervisor (nurse, physician, or physician assistant), DOT outreach workers, other staff providing direct patient care, and person managing the contact investigation
- Patient educator's name and dates of education sessions
- Method for prevention of transmission: no isolation, airborne infection isolation, home isolation, legal order for isolation
- Contract Treatment Agreement -signatures of the local health jurisdiction representative and the patient (or patient's representative)
    - Acknowledgement of Counseling (PHSKC)
    - Public Health Directive (Adherence) (PHSKC)
    - Public Health Directive (Non-Compliance) (PHSKC)
    - Authorization for Care Coordination (PHSKC)
    - Authorization for Disclosure of Protected Health Information (PHSKC)
    - Civil Detention Flowchart
- Planned course of antituberculosis drug therapy
- Estimated date of completion of treatment (i.e. treatment plan)
- Test results from initial medical evaluation
- Medical history
- Diagnosis
- Monitoring activities and schedule to assess response to therapy
- Baseline tests and monitoring activities and schedule to detect potential side effects and adverse reactions
- Potential drug interactions
- Potential treatment adherence obstacles
- Personal service needs
- Referrals for social services
- Process of ensuring successful completion of treatment (DOT, incentives, enablers)
- Location(s) where DOT and Video DOT will be administered and time of day
- Intermediate and expected outcomes[28]

For a list of intermediate and expected outcomes, see *Module 2:* "Fundamentals of TB Case Management," pages 23–25 in the New Jersey Medical School National Tuberculosis Center's *Tuberculosis Case Management for Nurses: Self-Study Modules* (New Jersey Medical School Global Tuberculosis Institute Web site) at http://www.umdnj.edu/globaltb/products/tbcasemgmtmodules.htm .

Planning Activities

To complete planning, perform the following activities:

- Establish the treatment plan
- Establish time frames in the treatment plan to monitor the plan and patient response
- Negotiate and adjust the treatment plan

Establish the treatment plan, ensuring that all the components are included. The case manager should ensure that the treatment plan is useful and meaningful. It becomes the internal standard of care for the patient as well as the performance standard for the case manager. Good planning will allow the patient to experience TB care and treatment along the healthcare continuum and prevent duplication and fragmentation of services. The plan should be discussed and validated with all team members and the patient.[29]

Directly observed therapy (DOT) is the preferred initial strategy of care for all TB cases and suspects. DOT and Video DOT, coupled with individualized case management, leads to the best treatment. DOT should be used for all patients residing in institutional settings (i.e. hospitals, nursing homes, correctional facilities) or other settings, such as methadone treatment sites. Priority situations for the use of DOT and Videophone DOT include children and adolescents and patients with the following conditions/circumstances:

- Pulmonary tuberculosis with positive sputum smears
- Treatment failure
- Drug resistance
- Relapse
- HIV infection
- Previous treatment of either active tuberculosis or latent tuberculosis
- Current or prior substance abuse
- Psychiatric illness
- Memory impairment
- Previous nonadherence to therapy

Establish time frames in the treatment plan to monitor the plan and patient response. Monitoring should be done at least monthly at the patient's home, ambulatory clinic, health department, or private physician's office. Each component of the plan should be reviewed to ensure that it is an accurate accounting of the patient's problems, required tests, and interventions. To track progress toward outcomes, document all treatment activities and their dates: medications taken, tests and results, patient visits, monitoring activities, side effects, adverse reactions, education sessions, social service referrals, incentives, enablers, isolation status changes, and patient problems.[30]

Negotiate and adjust the treatment plan as needed, to meet new realities. Since patient circumstances are usually fluid and personnel resources often change over time, it is essential that the plan be negotiated with the patient and changed to adjust to new situations. The adjusted plan should be discussed with the team members, as well as the patient.[31]

Implementation Activities

To begin implementation of the treatment plan, perform the following activities:

- Refer the patient to other healthcare providers, social service agencies, or community organizations, as needed, with the case manager functioning as a liaison
- Broker and locate needed services relating to TB treatment
- Negotiate a plan for evaluation of DOT, Videophone DOT or self-administration of medications
- Coordinate strategies to improve adherence

Refer the patient to other healthcare providers, social service agencies, or community organizations, as needed. The referral process requires the case manager to locate and coordinate accessible, available, and affordable resources for the patient. After the referral is made, the case manager should monitor the patient's adherence to the referral and obtain the consultation or follow-up report in writing. Immediate intervention may be necessary if the patient or the referring agency experiences difficulty.[32] All patients with suspected or proven TB should be tested for HIV infection, with referral for HIV treatment services when necessary. Referrals to medical specialists for conditions that would endanger the patient and/or affect the outcome of treatment should be made as soon as possible. The patient should be sent to an emergency department if the condition is serious when assessed by the case manager. The case manager should follow up a referral to obtain medical information and determine whether the necessary medical intervention has been completed.

Refer patient for services relating to the TB treatment if not available at the LHJ. This may include laboratory, auditory, or visual acuity testing; additional radiographs; or other tests required specifically for the patient. It is important to schedule or assist the patient in scheduling appointments and to monitor the patient's adherence to the appointment and the results.

An understanding of the patient's financial resources and health insurance coverage is important. [33] In Washington State, each LHJ is responsible for providing treatment of tuberculosis (both pulmonary and extra-pulmonary) if patients lack of financial resources or health insurance (see WAC-246-170-031).

Negotiate a plan for evaluation of DOT, Videophone DOT or self-administration medications. DOT is the preferred initial strategy of care for all TB cases and suspects. DOT and Videophone DOT, coupled with individualized case management, leads to the best treatment. The case manager should ensure the plan is suitable for the patient's needs and achievable by the healthcare provider(s) and then have the patient sign a DOT agreement. Due to the length of TB treatment, the patient's circumstances may change. The case manager needs to verify that the time and place for DOT administration originally agreed upon is still agreeable to the patient and provider. It also may be necessary to coordinate the arrangements for DOT with facilities outside the LHJ, such as school nurses, drug treatment center nurses, pharmacies, fire departments and employers.[34]

Refer to the "Directly Observed Therapy and Videophone DOT" topic in this section of the manual (**8.57**).

Coordinate strategies to improve adherence. The case manager must have knowledge of and proficiency in strategies to improve patient adherence, understand the importance of developing and maintaining a therapeutic relationship, and be familiar with the principles and practices of behavioral contracting and behavioral modification. Collaboration with team members is essential to obtain as much information as possible about strategies to improve adherence of individual patients and elicit opinions, attitudes, and feelings expressed by the patient. Depending on the identified obstacles to completion of therapy, the treatment plan may also include enablers and incentives (see MMWR Treatment of Tuberculosis, 2003, specifically p.17 table 8, at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf). To be effective, incentives and enablers should be meaningful and specific for a particular patient.[35] Incentives and enablers should be considered for use with all patients.

Ongoing Assessment and Monitoring

Conduct ongoing assessments and monitor patients at least monthly, either in an ambulatory clinic setting, LHJ or private physician's office. Schedule additional assessments throughout the month for patients experiencing problems in their tuberculosis (TB) treatment, or for those patients who are nonadherent to directly observed therapy (DOT), Videophone DOT or follow-up appointments.[36]

There are countless stories from nurses and outreach workers reinforcing the fact that not all information is obtained from the patient or family during the initial visit. Therefore, the case manager must ensure that the list of contacts is updated as follow-up visits are made to the patient and other contacts. The updated information is necessary to determine the need for further testing. It is important to review the status of the contact investigation to ensure that timelines and standards are followed. Additionally, checking for the accuracy of previously gathered information should occur throughout the patient's TB treatment.[37]

Ongoing Assessment Activities

To complete an ongoing assessment, perform the following activities:

- Determine human immunodeficiency virus (HIV) status and the risk factors for HIV disease, and refer the patient for treatment, if indicated
- Monitor the clinical response to treatment
- Review the treatment regimen
- Ensure that correct medications with correct dosage are ordered and given as per current American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines
- Monitor the side effects of and adverse reactions to medication
- Assess adherence daily and monthly, and identify positive and negative motivational factors influencing adherence
- Determine the unmet educational needs of the patient
- Educate the patient about the TB disease process
- Advocate for the patient with team members and other service providers
- Review the status of the contact investigation, if one was started

Monitor the clinical response to treatment by reviewing vital signs, weight, bacteriology reports, and radiographic results, including drug susceptibility results and TB symptoms, and comparing them to previous documented findings. This review is an important measurement of clinical improvement, worsening, or stabilization of the patient's condition. If the patient's condition is worsening, interview the patient to determine the potential cause(s) for the worsening condition. List all bacteriological reports in chronological order, and correlate them with the patient's current symptoms history and chest radiograph report(s) to ensure accuracy.

Also, conduct this review at conversion of both smear and culture as evidence for the improving condition of the patient.[38]

Inconsistencies should trigger additional questions, such as the possibility of laboratory contamination. Bring these questions immediately to the attention of the patient's medical provider, local health officer and WA State TB Services 360-236-3443.

A child's clinical response to treatment may not be as significant as that of an adult. Therefore, it is important to reinforce what the expected response to treatment should be for the individual child during the course of treatment and to weigh the child monthly. [39]

Determine HIV status and the risk factors for HIV disease, and refer the patient for treatment, if indicated. It is important for patients to understand the correlation between TB and HIV disease. The case manager should ensure that HIV counseling and testing are completed at the beginning of TB treatment, if the HIV status is not previously known. If the patient refuses HIV testing, an assessment of the risk factors for HIV should be completed.[40] If a patient refuses, voluntary HIV testing and counseling should continue to be offered periodically throughout treatment.

If the parents of a young child with TB refuse to permit the child to be HIV tested, the parents should be interviewed regarding the child's risk of HIV disease, including neonatal transmission.[41]

Review the treatment regimen to verify that the physician's orders are clear and concise. One of the case manager's primary responsibilities is to ensure that the patient completes treatment according to the physician's orders. It is also important to ensure that the plan is specific for the individual patient and follows the principles of TB treatment.[42] For questions regarding treatment, contact Washington State TB Services Medical Consultant at 206-718-2664.

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

Ensure that medications are ordered, in the correct dosage and given at the correct time. Review the patient's treatment plan and chart, and correct the medications as necessary.

Monitor the side effects of and adverse reactions to medication. Review laboratory findings and contact the treating physician if abnormal results are obtained.[43] The patient should be monitored by a registered nurse and/or clinician or case manager at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be immediately consulted and the patient monitored more frequently. Chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done periodically per

physician's order. See **monitoring and Interventions for "**Side Effects and Adverse Reactions**"** in the Treatment of Tuberculosis Disease section of the manual (**5.19**).

If a child is taking TB medications at school, communicate at a minimum on a monthly basis with designated staff to determine whether the child is experiencing medication side effects or adverse reactions.[44]

Assess adherence daily and monthly, and identify positive and negative motivational factors influencing adherence. An assessment of adherence needs to occur at each patient encounter. If the case manager is not involved in providing DOT or Videophone DOT, a notification system should alert him or her if the patient misses a DOT dose or if there is suspicion of nonadherence if the case is on self-administered therapy (i.e. via pill count or pharmacy checks). If a DOT or Videophone DOT dose is missed, the patient should be contacted the same day or the next business day and the issue escalated to the case manager's supervisor. Direct observation provides immediate information on poor adherence and adverse effects. The key to a successful DOT program is the timely use of this information in order to promptly identify and respond to potential barriers to adherence, missed doses, and potential adverse treatment effects. **It is important not to send a mixed message to a patient by not promptly responding to missed DOT doses**. If the patient is self-administering TB medications, make a weekly visit to the patient's residence to assess adherence and monitor for side effects and adverse reactions. Also, regularly monitor the effectiveness of enhancement methods (i.e., incentives, enablers, behavioral contracting, or behavior modification).[45] DOT and Videophone DOT is highly recommended if adherence is compromised (see MMWR Treatment of Tuberculosis, 2003, specifically p. 16, table 7, at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf).

The case manager should ensure that the patient is informed about the consequences of nonadherence, including legal interventions and has signed contracts of understanding between the patient and the LHJ, both regarding the treatment of TB and Videophone DOT. Changes in the patient's attitude toward the healthcare worker should be documented and verified with the patient.[46]

For more information, see the following topics in this section: "Directly Observed Therapy"(**8.51**) and "Legal Orders" (**8.59**). Also, see following forms:

- Acknowledgement of Counseling (PHSKC)
- Public Health Directive (Adherence) (PHSKC)
- Public Health Directive (Non-Compliance) (PHSKC)
- Authorization for Care Coordination (PHSKC)
- Authorization for Disclosure of Protected Health Information (PHSKC)
- Civil Detention Flowchart

Determine the unmet educational needs of the patient regarding transmission, diagnosis, and treatment of TB. Identify the concerns and anxieties regarding diagnosis, and need for further education. The educational needs of the patient/family may vary throughout the course of treatment. Patient education also will vary depending on beliefs about TB treatment, acceptance of the diagnosis, coping mechanisms, cultural values, and the accuracy of the information they have already received. The case manager should explore the effect the diagnosis has on the patient's relationships with other family members, coworkers, and social contacts so that appropriate, culturally sensitive information can be provided.[47]

Educate the patient about the TB disease process during the course of TB treatment. Provide instruction relevant for the patient's level of education or ability to learn, and address healthcare beliefs that are in conflict with educational information. The case manager should ensure that education is provided in the patient's primary language and that it is culturally appropriate.[48] The case manager should provide patient and family education monthly, until satisfactory recall is obtained.

For more information, see the Patient Education section of the manual (**15.1**).

Advocate for the patient with team members and other service providers when necessary. The case manager should demonstrate respect and understanding of the patient's cultural beliefs and values, and prevent team members from imposing their own values or belief systems on the patient. The case manager should be able to communicate the patient's fears/anxieties, likes/dislikes, and needs/wants to the team members in a nonjudgmental manner. The case manager must also have an understanding of the team members, and mediate, negotiate, and resolve differences of opinion regarding the patient and interventions.[49]

Review the status of the contact investigation, if one was initiated. It has been found that patients may not initially reveal the names of all close contacts. Over time, many more individuals are often identified.[50]

The investigation should be repeated if for any reason the index patient becomes AFB sputum smear positive again during treatment and there has been sufficient exposure for the skin-test-negative or IGRA negative persons to become infected.

Monitoring Side Effects and Adverse Reactions

Assess and document side effects and adverse reactions to antituberculosis medications and monitor toxicity. The patient should be monitored by a registered nurse and/or clinician or case manager at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be consulted immediately and the patient monitored more frequently. Chemistries and CBC, AST/ALT, or other tests based on specific drugs should be done periodically. See "Side Effects and Adverse Reactions" in the Treatment of Tuberculosis Disease section of the manual (**5.19**). As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.[51]

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that first-line drugs not be stopped without adequate justification.[52] However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy, whereas with more severe effects, the offending drug or drugs must be discontinued.[53] In addition, proper management of more serious adverse reactions often requires expert consultation.[54] Washington State TB Services Medical Consultant at 206-718-2664 is available upon request.

Instruct patients to report the side effects and adverse reactions listed in the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section of the manual (**5.19**).

To monitor for side effects and adverse reactions, perform the following activities:

- Educate the patient and family to report side effects and adverse reactions
- Assess the patient at least monthly for side effects and adverse reactions

Educate the patient and family to report side effects and adverse reactions. The case manager reinforces prior patient teaching and continues to educate the patient and family about TB medications, signs and symptoms of adverse effects, and the importance of continued treatment and uninterrupted drug therapy. Case managers should be familiar with all TB medications, their side effects, contraindications, and drug interactions.[55]

For more information, see the Patient Education section of the manual (**15.1**).

Assess the patient for adverse reactions and side effects. For patients receiving DOT and Videophone DOT, staff should assess them for side effects and adverse reactions on each visit by performing a symptom review. If indicated, order liver function tests and monitor their results. The case manager should be aware of complications in patients on medications by maintaining close communication with outreach staff providing the DOT for patients on self-administered therapy, the case manager ensures that patients are assessed for side effects and adverse reactions to TB medications at least monthly and at each visit.[56]

Monitoring Bacteriologic Improvement

Sputum Smears and Cultures

During treatment of patients with pulmonary TB, a sputum specimen for microscopic examination and culture should be obtained at a minimum of monthly intervals until two consecutive specimens are negative on culture and then monthly for remainder of treatment. More frequent acid-fast bacilli (AFB) smears may be useful to assess the early response to treatment and to provide an indication of infectiousness. For multidrug-resistant TB (MDR-TB) and extremely-drug-resistant TB (XDR) patients, monthly specimens are required. For patients with "Extrapulmonary TB" (**10.22**) the frequency and types of evaluation will depend on the site involved.

Activities to Monitor for Bacteriologic and Clinical Improvement

If the patient initially had positive AFB sputum smear results quantified as 1+ to 2+, collect one sputum specimen per week and submit it for testing until one specimen tests negative. After the specimen tests negative, then obtain two more consecutive sputum specimens collected 8 to 24 hours apart, with at least one being an early morning specimen (see MMWR Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005, specifically "Sputum Specimen Collection", p. 51).
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

If earlier AFB sputum smears were positive and now AFB sputum smears are negative on three separate, consecutive days, consider discontinuing isolation.[57]

For patients with culture-positive pulmonary TB, collect at least one sputum specimen for smear and culture until persistently negative cultures are documented.[58] See "TB Lab Flow Chart" to view the PHL Algorithm.

Continued Positive Sputum Smears or Positive Cultures

A patient with continued AFB sputum smear positive results or positive cultures should be evaluated for treatment failure if sputum specimen(s) remain bacteriologically positive (i.e., culture positive and/or AFB sputum smear positive) after three months of treatment or become bacteriologically positive after initially converting to negative.

The case manager should initiate the evaluation of the patient and notify his or her supervisor immediately. The case manager should also do the following:

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

1. Review and confirm the patient's medication adherence.
2. Place the patient on DOT, if not already on DOT.
3. Reconfirm the appropriateness of the medication regimen, based on drug susceptibility results and other considerations.
4. Consultation with a provider experienced with TB relapse and/or failing regimens is highly recommended. Washington State TB Services Medical Consultant is available at 206-718-2664.
5. If additional antituberculosis drugs are added to the treatment regimen, ensure that at least two new drugs that the patient has not been treated with previously are used. **Never Add a Single Drug to a Failing Regimen**.
6. Consider serum drug levels.
7. Repeat cultures and repeat drug susceptibility testing.

Culture Negative or No Specimens

If a patient is culture negative or no specimens were collected:

1. Review the medications that the patient was on at the time TB medications were started, particularly other antibiotics.
2. If applicable, obtain follow-up chest radiograph reports to determine status, i.e. improving, worsening, or stable.
3. Review the patient's symptoms and weight for improvement, if applicable.
4. Review the patient's tuberculin skin testing or IGRA testing information (retesting may be appropriate if initially negative or test not initially done), and discuss this with the patient's medical provider.
5. Review information with the provider regarding his or her reasons for continuing TB medications.
6. Discuss the above findings with the LHJ health officer to determine if the patient is to be reported as a case.

Verification of Isolate Drug Susceptibility Results

The case manager should obtain and promptly document all positive cultures and respective drug susceptibility results.

1. **If a patient's TB organism is pan-susceptible:** Follow the recommended treatment regimen.
2. **If a patient's TB organism is drug resistant,** consult with patient's medical provider, local health officer, or Washington State TB Services Medical Consultant at 206-718-2664.

3. **If isoniazid-resistant, multidrug-resistant TB (MDR-TB) or extremely drug resistant TB (XDR-TB):** Treatment of LTBI caused by drug-resistant organisms should be provided in close consultation with an expert in the management of these difficult situations. For patients with MDR-TB or XDR-TB contact Washington State TB Services Medical Consultant at 206-718-2664 in consultation with the local health officer.

Multidrug-Resistant Tuberculosis

If a patient has MDR-TB, the case manager should:

1. Notify his or her supervisor and the patient's provider the same day that MDR-TB findings are reported/known.
2. For consultation regarding the treatment of drug-resistant TB, contact the Washington State TB Services Medical Consultant at 206-718-2664.
3. Initiate transfer of patient care to a more appropriate provider, if necessary. The case manager, with TB clinician/ Washington State TB Services Medical Consultant, should confer with the provider and arrange transfer of the case to a provider with experience/expertise in the management of MDR-TB. The case manager must document transfer of care and ongoing follow-up.
4. Obtain appropriate medications from suppliers.
5. Initiate DOT and maintain accurate DOT records. If the patient is nonadherent with DOT, the case manager must document attempts to correct the situation and notify his or her supervisor.
6. Provide the following for patients with MDR-TB:
   - Patient education, including information regarding second-line TB drugs
   - DOT at the patient's convenience
   - Incentives and enablers
   - Legal orders

For more information, refer to the Patient Education section and topics in this section on "Directly Observed Therapy, Incentives and Enablers" and "Legal Orders."

Clinical Response to Treatment

The case manager should monitor/evaluate a patient's clinical response to treatment. The following are indicators of a patient's clinical response to treatment:

- Lessening or resolution of TB symptoms
- Weight gain
- Progressive improvement in the chest radiograph (if pulmonary TB disease is diagnosed and repeat radiographs are ordered)

Isolation

If a patient is isolated, ensure and document the patient's adherence to respiratory isolation. [59]

For more information on isolation and quarantine, refer to the Infection Control section.

Closing a Case

If the patient is not to be reported as a case, notify the provider that the patient is closed to TB control program services. The patient can be closed to TB Registry.

For more information on closing a case, see the "Completion of Therapy" topic in this section.

Completion of Therapy

The case manager should verify completion of therapy. Completion of therapy is essential to ensure that the patient is cured. It is also a State of Washington and Centers for Disease Control and Prevention (CDC) goal and important measurement of the effectiveness of tuberculosis (TB) control efforts. Verification of completion of therapy and a completed contact investigation are the responsibility of the case manager.

Record verification and closure information in TB PHIMS. For more information, see the TB PHIMS User Manual at http://www.doh.wa.gov/Portals/1/Documents/Pubs/343-099-PHIMSTBUserManual.pdf

Verifying Adequate Course of Treatment

Most cases of active TB can be successfully treated using the standard short course (six months) of therapy. The case manager is responsible for considering the following conditions to ensure that the patient has received an adequate course of therapy.

For more information regarding Protocol and Standing Orders for local health jurisdictions, please see "Protocol and Standing Orders" located in the **FORMS** section of the manual.

- **If culture remains positive beyond two months of treatment,** reasons for persistent positive cultures should be examined and treatment adjusted and/or prolonged.
- **For TB involving the bones or joints or tuberculous meningitis:** These are exceptions to the standard six-month course. See "Bone and joint tuberculosis" and "Tuberculosis meningitis" in the "Treatment in Special Situations" (**5.32**) section of Treatment of Tuberculosis Disease of the manual or MMWR Treatment of Tuberculosis at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm
- **HIV-negative, culture-negative patients:** MMWR Treatment of Tuberculosis at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm
- **Relapse of TB following treatment for TB with pan-susceptible organisms.** (Current drug susceptibility testing must be performed and the regimen adjusted if resistance has developed.)[60] See "Management of Relapse, Treatment Failure, and Drug Resistance" http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

Calculating Completion of Therapy

So that doses missed due to nonadherence or other treatment interruptions are still given after treatment is resumed, the 2003 revised TB treatment guidelines "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf recommend basing the completion of treatment on the number of doses of directly observed therapy (DOT) received rather than on the chronological passage of time (e.g., six months).[61]

For the total number of doses recommended for completion of regimens using first-line drugs, refer to the "Recommended Treatment Regimens", specifically "Definition of Completion of Therapy" (pg.40) in the Treatment of Tuberculosis Disease at .
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

Closures Other than Completion of Therapy

- **Moved:** The case manager should obtain the new or forwarding address. Complete and submit copy of the Interjurisdictional Tuberculosis Notification form, to both the receiving site and Washington State TB Services. If possible, this form should be submitted to both the receiving site and DOH prior to the patient's move. Cases should be closed as "moved" **only** if a new address is obtained.
- **Not TB:** If the completed diagnostic evaluation determined that the diagnosis of TB is not substantiated and another diagnosis is established, the case is closed as "Not TB".
- **Died:** If the patient expired prior to completion of therapy, the case is closed as "Died."[62] The LHJ should provide the date of death on the completion of therapy report and also indicate if death was "TB related death" or "Non-TB related death". Submit the completed form WA State TB Services. Note in the PHIMS TB "comment section" if death was TB related or not.

Ensure that the contact investigation on the case is also completed. For more information see Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis at
http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Evaluation

Evaluate case management activities. Patient care is never complete without the evaluation component. In tuberculosis (TB) case management, the achievement of desired outcomes must be evaluated so that services and activities can be improved and TB treatment goals achieved. Evaluation is the outcome of the case management process and should be continuous and ongoing.

Evaluation activities answer the following questions:

- Were the TB treatment plan and control activities implemented in a timely manner?
- Were intermediate and expected outcomes achieved?
- Was the patient satisfied with services or care?
- Were the case manager and the team members satisfied with the plan and outcomes?

To evaluate case management, perform the following activities:

- Review the patient's record (i.e., medications, bacteriology, radiographs, patient status, and etc.) and Update Reports sent to Washington State TB Services
- Review Cohort Review Report
- Review the contact investigation

Review the treatment plan at least monthly, or more frequently, depending on the complexity of treatment and patient variables. Review the appropriateness of interventions, as well as dates when intermediate and/or expected outcomes were achieved. Pay attention to how rapidly the treatment plan was changed when the need was identified (i.e. timeline). If the treatment plan has remained unchanged, determine the reason why.[63]

Review reports and the contact investigation to ensure that the TB case reports are accurate and updated and that the contact investigation is complete.[64]

TB Staffing Standards

Tuberculosis programs throughout the Country are struggling with developing staffing standards. There is no standardized way of determining how many nurses, outreach workers, disease investigators, or medical support staff are required to do TB control. On face value this may appear to be a very simple computation, but in reality is not. Determination of staffing levels for TB programs is compounded by many issues, including, but not limited to:

- Multiple risk factors associated with a large percentage of TB clients
- Travel distance in rural areas and/or traffic congestion in urban areas
- Cultural issues
- Communication issues
- Acceptance of diagnosis
- Length of treatment
- Prevalence of drug-resistant TB
- Partnership and private sector

Even with this type of information many administrators and policy makers continue to question the amount of staffing required in TB control programs. What many of them fail to understand is that for every active TB patient there is an average of seven to ten contacts. There may be substantially more if there is a work, institutional, or school exposure. Each of these contacts must be assessed for signs and symptoms of TB skin tested and/or referred for testing and or chest radiograph and medical examination.

Additionally, there are many individuals who are referred to a TB control program who are suspects. They must be assessed and case managed as if they have active TB disease until lab tests and or/clinical diagnosis rules this out, but are not counted in the number of confirmed cases which is what usually drives staffing levels and TB control programs. Further it deemed necessary, contact investigations will be done for “TB suspects”.

This may seem complicated enough, but thus far we have not even taken into consideration the prevention aspect of TB control. More than 16,000 new cases of TB disease still occur each year in the United States, and an estimated 10-15 million persons have latent TB infection with the attendant risk of future disease. To effectively eliminate TB these infected individuals must be identified and treated. Such prevention and control interventions are beyond the scope of many TB control programs in the United States. Most programs are struggling to cope with the workload created by individuals with active disease and have no, or minimal resources for effective prevention interventions.

If all the facets of TB control are considered what may seem like a small number of clients mushrooms into a substantial workload. We must be able to capture the nature of this work and translate it into a staffing standard that definitively defines the number of staff required to do all aspects of the work.

The National TB Controllers Association and the National TB Nurse Consultant Coalition recognized this as a major concern and in September 1999 created a joint NTCA/NTNC Staffing Standards Committee to develop a methodology to determine staffing standards for TB Control. The Committee consisted of eight TB nursing experts from four different states and was representative of both urban and rural programs. The Committee has worked diligently to develop and test instruments that can be used to determine required staffing levels in TB Control programs and completed a nine month multi-state trial of these instruments in 2004.

For training and assistance with the tools provided please call the Washington State TB Services 360-236-3443 or email at tbservices@doh.wa.gov.

TB Staffing Standards Model (Forms Section)

Cohort Review in Washington State

History

The 2000 Institute of Medicine report *Ending Neglect: The Elimination of Tuberculosis in the United States* concluded that tuberculosis (TB) elimination is feasible, but will require "aggressive and decisive action beyond what is now in effect." The report recommended adopting an aggressive strategy in order to maintain control and ensure the most efficient application of resources. To this end, TB control programs must develop new standards by which to monitor and evaluate program performance[65].

One such evaluation method is cohort review, a systematic review of patients with TB disease and their contacts. A "cohort " (which can be defined as "a group of individuals having a statistical factor , such as age or disease in common' in a demographic study) of tuberculosis patients is reviewed in terms of each individual patient and contacts outcomes, as well as for program performance. Cohort review is a management process used to motivate staff, identify program strengths and weaknesses, determine staff training and professional education needs, and hold staff accountable for completion of treatment for both TB disease and latent TB infection (LTBI) [65].

The cohort review process can take many forms. In its most simplified form, TB control staff at the local level meet to review the treatment outcomes of every patient listed in a chronological patient register. Today, with computerized TB registries, multimedia projection, and long-distance communications options, it can be adapted for a variety of uses and settings[65.]

Washington State Medical Case Review / Cohort Review Process

Washington adopted the cohort review process in 2003 based on the New York City model, which was then modified a year later to meet specific WA State needs. Since then Cohort Review has become an integral part of the TB Program. However in late 2010, due to budget cuts, staffing time and dissatisfaction with the process, a workgroup was formed to revise and develop an improved case management and cohort review process that will better suited to meet our state's needs. Ideas that were proposed by the workgroup and subsequently implemented by the TB Program include:

- Reviewing cases in real-time – Medical case management oversight
- Eliminating the cohort review presentation forms – capturing all necessary data in PHIMS TB
- Changing quarterly format from retrospective cohort review presentations to a clinical review of open, counted cases
- Incorporating biannual program evaluation (based on core objectives and measures) with a review of selected cases with a pre-selected cohort criteria
- Making the process more effective, efficient, and interactive

In January 2012, the Medical Case Review / Cohort Review Process (formerly known as just the Cohort Review Process) was implemented. The following table shows what the new, two part, process looks like.

Medical Case Review / Cohort Review 2012

The following definitions may be helpful in this new process:

- **Case Review** – Discussion of patient case management; report on clinical status of the patient and identify variances/barriers in progress.
- **Quality Assurance** – A program for the systematic monitoring and evaluation of the various aspects of a project or program to ensure that standards of quality are being met.
- **Cohort Review** – A systematic, retrospective review of the management and outcomes of patients with TB disease and their contacts.

***Quarterly* Medical Case Review**	***Bi-annual* Cohort Review**
Attendees: • DOH Medical Consultant • LHJ Representative(s) • DOH Nurse Consultants	*Attendees:* • DOH Medical Consultant • DOH TB Program • DOH Epidemiologist • All LHJs • Other interested parties
DOH will organize conference call by: • Pulling a list of current cases from PHIMS TB two weeks prior to case review date • Providing LHJs and DOH Medical Consultant with a list of the RVCT numbers of current open cases that will be reviewed • Emailing an agenda to LHJs with current cases stating their case will be reviewed and provide a time frame of when DOH will contact them	*DOH will organize meeting by:* • Two months prior to Cohort Review researching cases and selecting a limited number to be presented • One month prior to cohort review date contacting the LHJs with selected cases to offer the option of presenting their case or having DOH present • Emailing all attendees the agenda/meeting information to attend via webinar or in-person • Providing each LHJ a copy of county-specific data for use in assessing how their LHJ is meeting core indicators
During the call: • Each case and their contacts will be reviewed in PHIMS TB with LHJ staff and DOH during a brief discussion • DOH Medical Consultant/DOH Nurse Consultants will provide recommendations/follow-up for cases and contacts as needed	*During the meeting:* • DOH will present data on core indicators for Washington State • Facilitated discussion of issues identified related to case management • Presentation by LHJ or DOH of the selected cases and interactive discussion of cases

During the biannual Cohort Review, the epidemiologist will report on a variety of timeliness measures as well as focusing on the following six core indicators:

- Cases who complete treatment in 12 months
- Sputum culture conversion
- Time from sputum smear positive result to starting TB treatment
- Treatment failures and relapse rates
- Contacts evaluated
- Contacts who start/complete treatment for LTBI

Directly Observed Therapy

Provide directly observed therapy (DOT) or Videophone-DOT, as required. DOT means that a healthcare worker or other designated individual trained by the local health jurisdiction watches the patient swallow every dose of the prescribed TB drugs ("supervised swallowing"). A family member should not be designated to observe therapy. A dose of medication that is delivered to a patient, an address, or a mailbox or left with a family member, friend, or acquaintance is a dose of self-administered therapy (SAT) and should be designated as such.

DOT is a component of case management that helps to ensure that patients receive effective treatment and adhere to it. The American Thoracic Society (ATS), the Centers for Disease Control and Prevention (CDC), and the Washington State Department of Health recommend that every tuberculosis (TB) patient be considered for DOT.[66] DOT is implemented because

- DOT is the most effective strategy for making sure that patients take their medicines;
- DOT can lead to reductions in relapse and acquired drug resistance;[67] and
- Directly observing each dose provides immediate information on poor adherence and adverse effects, information that cannot readily be obtained from patients treated with SAT.

Candidates for Directly Observed Therapy

DOT *should be* the standard of care for all TB cases and suspects. In Washington State, DOT *is* the standard of care, that is, it is our goal to place all patients on DOT regardless of the patient's circumstances, because it has been shown to be such an important treatment tool.[68] Priority situations for the use of DOT include TB cases and suspects with the following conditions/circumstances:

- Pulmonary tuberculosis with positive sputum smears
- Children and adolescents
- Treatment failure
- Drug resistance
- Relapse
- HIV infection
- Previous treatment of either active tuberculosis or latent tuberculosis
- Current or prior substance abuse
- Psychiatric illness
- Memory impairment
- Previous nonadherence to therapy

All patients being treated with regimens that use intermittent drug administration have all doses administered under DOT because of the potentially serious consequences of missed doses (see Treatment of Tuberculosis, "Promoting Adherence", p. 16).
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

DOT for Contacts Receiving Treatment for Latent TB Infection (LTBI): One of the national health objectives for 2010 is to complete treatment in 85% of contacts who have latent TB infection (LTBI). Washington State and the nation have fallen short of national objectives. To increase these rates, CDC recommends focusing resources on the contacts most in need of treatment, monitoring treatment (including contacts receiving care outside the LHJ) and providing DOT (see Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, "Treatment for Contacts with LTBI", pg. 16).
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a1.htm

How to Deliver Directly Observed Therapy

For an example job description outlining duties of DOT worker, go to:
http://www.doh.wa.gov/Portals/1/Documents/Pubs/343-Non-PositionDescription.pdf

Who Can Deliver Directly Observed Therapy (DOT) and Videophone-DOT?

- TB clinic personnel or other healthcare workers trained by the LHJ to provide DOT.
- Staff at other healthcare settings, such as outpatient treatment centers
- Facilities outside the LHJ, such as school nurses, drug treatment center nurses, pharmacies, fire departments and employers. .
- *Not* family members[69]

Principles of Directly Observed Therapy (DOT) and Videophone-DOT

- The healthcare worker, or whoever is providing the DOT, should watch the patient swallow each dose of medication.
- Use DOT with other measures to promote adherence such as enablers and incentives, see Treatment of Tuberculosis, "Promoting Adherence", Table 8, pg. 17.
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm
- DOT can be given anywhere the patient and LHJ agree upon, provided the time and location are convenient and safe.[70,71]

Directly Observed Therapy Tasks (in Person)

1. Deliver medication.
2. Check for side effects and adverse reactions.
3. Verify medication (by person providing DOT).
4. Have the patient verify the medication
5. Watch the patient take pills.

DOT Resources (**8.61**)

Healthcare workers should watch for tricks or techniques some patients may use to avoid swallowing medication, such as hiding pills in the mouth and spitting them out later, hiding medicine in clothing, or vomiting the pills after leaving the clinic.

If it is necessary to make sure that the patient swallows the pills, the healthcare worker may have to check the patient's mouth, or ask the patient to wait for a half hour before leaving the clinic so the medication can dissolve in the patient's stomach.[72]

6. Document the Visit

- Videophone Directly Observed Therapy Form (TPCHD) (Forms)
- Guidelines for Use of Videophone for DOT and DOPT (SHD) (Forms)

7. As necessary and appropriate, do the following:
   1. Provide patient education
   2. Help the patient keep appointments
   3. Connect the patient with social services and transportation
   4. Draw upon familiarity with the patient's home environment to identify household contacts
   5. Offer incentives and/or enablers to encourage adherence[73]

- For more information, refer to the “Incentives and Enablers” (**8.58**) topic in this section of the manual or “Treatment of Tuberculosis” http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf

Videophone Directly Observed Therapy (VDOT) Tasks

1. Videophone Directly Observed Therapy Form (TPCHD)

   Guidelines for Use of Videophone for DOT and DOPT (SHD)

2. Follow same process as DOT tasks, i.e. have patient verify medication, observe patient swallowing the medication, and document the event.

The article titled “Videophone utilization as an alternative to directly observed therapy for tuberculosis“ was written by our colleges from DOH, Snohomish Health District, and Tacoma Pierce County Health Department TB Programs. Abstract available at http://www.ingentaconnect.com/content/iuatld/ijtld/2010/00000014/00000006/art00019

Adherence to Directly Observed Therapy

Patient Education

The case manager should ensure that education is provided in the patient’s primary language and is culturally appropriate.[74]

For more information, see the Patient Education section. For points to use to explain to the patient why DOT is important, refer to the CDC’s *Questions and Answers About TB 2005. Active TB Disease: What is directly observed therapy?* (Division of Tuberculosis Elimination Web site; 2005) at http://www.cdc.gov/tb/publications/faqs/qa_TBDisease.htm .

Children with Tuberculosis

To facilitate DOT adherence of children with TB, the case manager needs to be familiar with the childhood developmental stages, including important events, and utilize strategies in consideration of these stages.

For more information on adherence strategies for different developmental stages, see Appendix C in the New Jersey Medical School National Tuberculosis Center's *Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider* (New Jersey Medical School Global Tuberculosis Institute Web site; 2004) at http://www.umdnj.edu/ntbcweb/products/mgmtltbi.htm

Agreements

It is recommended to develop a letter of agreement or acknowledgment between the patient and the local health jurisdiction (LHJ). Many LHJs in Washington State have successfully used Videophone DOT (VDOT) as a method of ensuring adherence to therapy. The DOT worker and the patient negotiate dates, places, and times for DOT services to be provided, and both sign a document stating such agreements. Included in the agreement could be language specifying what consequences may result in the event that the client violates the terms of the contract.[75]

- Videophone Directly Observed Therapy (DOT) Consent Form
- Direct Observed Therapy Agreement

Incentives and Enablers

Incentives and enablers may be appropriate to help patients adhere to DOT.

For more information, see the "Incentives and Enablers" topic in this section of the manual (**8.59**).

Missed Directly Observed Therapy Dose

If a DOT dose is missed, the patient should be contacted on the same day or on the next business day and the issue escalated to the case manager's supervisor.

It is important not to send a mixed message to patients by delaying the response to missed DOT doses. After telling patients that TB treatment is so important for their health and the health of the community, you cannot delay in responding to the failure to be available for DOT.

A missed dose needs to be seen as an opportunity to identify barriers to adherence and work with patients to find ways to successfully complete treatment. The key to a successful DOT program is the use of immediate information on poor adherence, side effects, and adverse reactions in order to promptly identify and respond to potential barriers to adherence, missed doses, and potential adverse treatment effects. This approach has been referred to as enhanced DOT—the use of a patient-centered approach to promptly identify and address barriers to treatment completion through use of incentives, enablers, and educational efforts appropriate to the individual patient.

Directly Observed Therapy/Videophone

Background

Directly observed therapy (DOT) for tuberculosis increases patient adherence. This increased adherence both reduces the risk of disease recurrence and also prevents the development of drug-resistant Mycobacterium tuberculosis strains.

DOT can be resource intensive and a burden to under-funded public health departments. Costs include personnel time and travel expenses.

The use of Videophone technology in selected patients provides DOT at a decreased cost while maintaining the benefits.

Application

Ideal candidates are those living at a considerable distance from the health department, those who will require therapy at atypical times and those who may require prolonged daily therapy. All potential patients will receive their initial four weeks of DOT through standard in-home visits.

All patients who agree to participate in Videophone DOT will sign a consent form and a statement of responsibility for the videophone equipment. Training on the videophone will be over two treatment days. During both of these days a health worker will be present in the patient's home to assist with the equipment and to provide practical instruction in its use.

During remote DOT, a monthly supply of pre-packaged medication doses will be given to the patient at each clinic visit.

The Local Health jurisdiction personnel will arrange a set time for the remote video call with the patient. During the video call the patient will be expected to display the medications onscreen. The health worker will then witness the patient swallowing the medication.

Exclusion Criteria

- Lack of land line telephone at patient location
- Less than 90% compliance with therapy during the initial four weeks of standard DOT
- Inability to maintain effective communication via the videophone either due to patient disability or language barriers
- Inability of the patient to demonstrate effective use of the equipment during the two-day training period.

Available Forms:

- DOT Audit Tool
- Policies and Procedures Inventory
- Policies and procedures request
- Report of Lost/Stolen
- VDOT Consent
- VDOT Tacoma-Pierce
- VDOT Snohomish
- VDOT Release of Liability
- VDOT Memorandum

Incentives and Enablers

Use incentives and enablers to enhance adherence to therapy.[76] Incentives and enablers are used to improve patient attitudes and to foster good health behaviors.[77] They help patients stay with and complete treatment.[78]

Incentives are small rewards given to patients to encourage them to either take their own medicines or keep their clinic or field directly observed therapy (DOT) appointments.[79] **Enablers** are those things that make it possible or easier for the patients to receive treatment by overcoming barriers such as transportation difficulties.[80]

Use of incentives and/or enablers should be considered for all cases of tuberculosis (TB) as an adherence-improving measure. The local TB case manager should determine the most appropriate incentive and/or enabler on a case-by-case basis. Some **examples** of incentives and enablers used previously are listed below.

TABLE 1: AVAILABLE INCENTIVES AND ENABLERS

Incentives	Enablers

• Food and beverages
• Clothing
• Automotive supplies
• Hobby/craft items
• Household items
• Laundry services
• Seasonal/holiday treats
• Movie passes
• Restaurant/fast food vouchers
• Toys
• Personal care items
	• Transportation
	  • Bus pass
	  • Cab fare
	  • Battery for patient's car
	  • Gas
	  • Fee for driver's license
	• Childcare
	• Obtaining and transporting specimens for the patient
	• Assisting the client to get medication refills
	• Rent assistance
	• Assisting the client to complete paperwork to get food/housing assistance
	• Assisting the client to get substance treatment

Legal Orders

For Washington State laws and rules on tuberculosis (TB) and Due Process, see the following: RCW 70.28.032 Due Process.

Understand when and how to use legal orders, if necessary, for adherence to therapy. Nonadherent adults with pulmonary TB pose the greatest threat to the health of a community. It is the local health jurisdiction's responsibility to ensure that compliance is maintained, treatment is completed, and the risk of transmission to others is eliminated. These responsibilities require that TB staff members be innovative and always "go the extra mile" to see that patients take their medicine as prescribed. The public health mandate and good judgment dictate that program staff should go to every extent possible to fulfill the job responsibilities outlined above before resorting to legal action.[81]

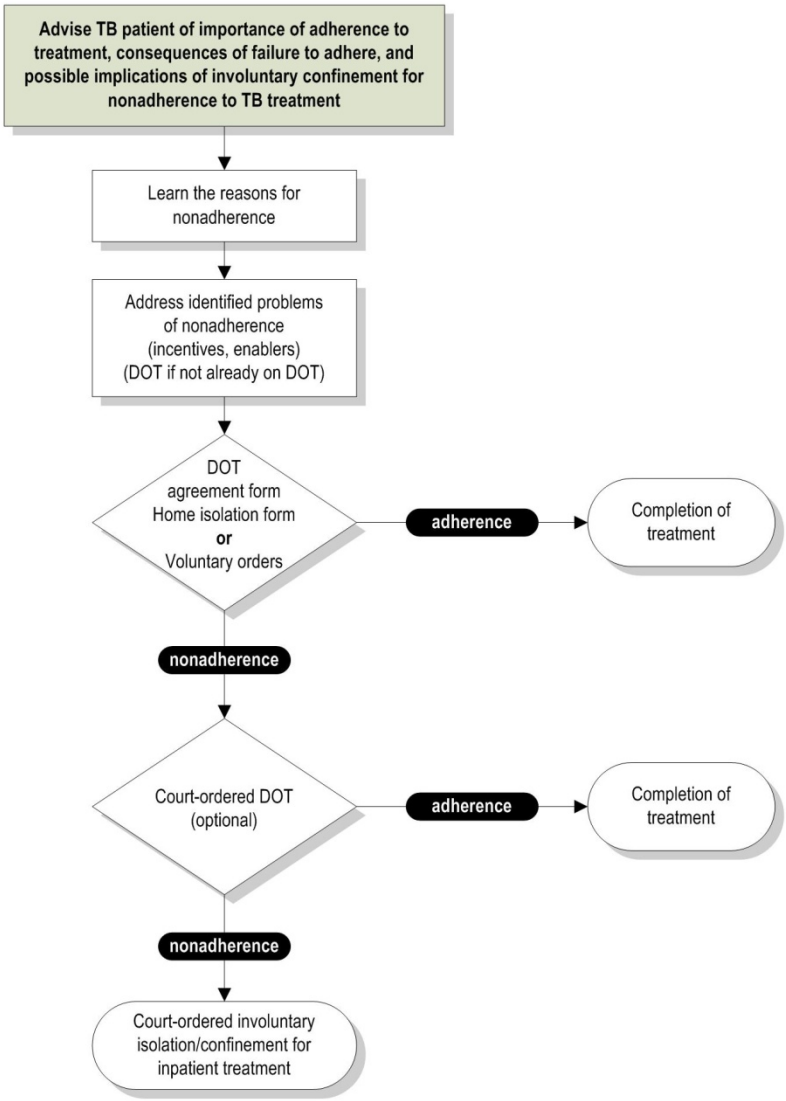
Have an intervention plan that goes step-by-step from voluntary participation to involuntary confinement as a last resort. Refer to Figure 1: Progressive Interventions for Nonadherent Patients. Progressive intervention should begin with learning the possible reasons for nonadherence and addressing the identified problems using methods such as directly observed therapy (DOT) and Videophone DOT (VDOT), incentives, and enablers. Prior to initiating treatment, the patient should be told verbally and in writing of the importance of adhering to treatment, the consequences of failing to do so, and the legal actions that will have to be taken if the patient refuses to take medication.[82] Thus, it is important to ensure an interpreter is provided during this process, if indicated.

Before legal measures are taken with a patient who has been taking TB drugs on a self-administered basis, DOT and/or Videophone DOT should be offered to the patient.[83]

Use a DOT or Videophone DOT agreement form and home isolation form with a patient who is likely to comply with treatment requirements. With a patient who may need more encouragement to adhere to treatment, complete a voluntary orders form. Voluntary orders are not legal orders but serve to clarify the mutual understanding between the patient and the local public health agency and provide written proof that treatment requirements were communicated to the patient and that the patient agreed to them.

If the patient does not adhere to DOT and/or Videophone DOT voluntarily, the next step may be court-ordered DOT. An optional step toward other legal orders, court-ordered DOT can be successful in convincing a patient that his or her TB treatment is an important public health priority. Involuntary confinement or isolation for inpatient treatment should be viewed as the step of last resort, to be used only when all other options fail. However, when a patient with infectious TB refuses treatment and voluntary isolation, emergency detention to isolate the person is appropriate.[84]

FIGURE 1: PROGRESSIVE INTERVENTIONS FOR NONADHERENT PATIENTS[85]



Definitions of abbreviations: DOT = directly observed therapy; TB = tuberculosis.
Source: CDC. Module 9: Patient Adherence to Tuberculosis Treatment. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:28.

Resources and References

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Directly Observed Therapy Resources

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Incentives and Enablers Resources

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Legal Orders Resources

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DOH 343-071 June 2012
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Contact Investigation

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Forms Used in this Section

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- Contact Investigation Instructions
- Health Advisory (Clark/Cowlitz/Skamania/Wahkiakum Counties)
- Protocol and Standing Orders (SHD)

Quick Start Check List: Contact Investigation

This check list is designed to assist public health nurses in conducting a contact investigation. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Contact Investigation	Instructions and Forms
Decide whether to initiate a contact investigation: ☐ Evaluate the index patient ☐ Gather the index patient's medical records (from hospital, clinic, and/or healthcare provider) ☐ Decide if a contact investigation is indicated ☐ If an investigation is indicated, start the contact investigation within ≤1 business day of the case report ☐ Submit the "Tuberculosis Contact Investigation Form" to WA State TB Services within 2 weeks **Note:** Contact investigations are conducted for persons with suspected or confirmed pulmonary, laryngeal, or pleuropulmonary tuberculosis (TB) disease with the following: • Pulmonary cavities and/or • Respiratory specimens positive for acid-fast bacilli (AFB) sputum smear	**Instructions:** Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions
Determine the time frame for potential exposure: ☐ Determine the start of the index patient's infectious period	
Interview the index patient: ☐ Conduct the first interview within ≤1 business day of the case report ☐ Visit the index patient's residence within ≤3 business days after first interview, if not already done in the first interview ☐ Reinterview the index patient within 1 to 2 weeks after the first interview ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions

Tasks for Contact Investigation	Instructions and Forms
During the interviews, gather information regarding the following: • Additional medical history • Residence(s) • Transmission sites, with dates and times • Contacts	**Note: The interviews for contact investigation also gather data for the initial assessment in case management and provide patient education**
List and prioritize contacts: ☐ During the index patient interview, list names and locating information of named contacts (plan to update this list throughout the investigation) ☐ Assign an initial priority classification to each contact (plan to revise as needed when new information is received) ☐ Review all documentation to ensure that the contact list is complete ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions
Complete the field investigation: ☐ Visit all potential transmission sites within 5 days after starting the investigation ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions
Start contacts on treatment for LTBI: ☐ Assure that treatment for LTBI is started for high-priority and high risk contacts (children under 5 years of age and persons who are at high risk of developing active TB disease) within 5 business days after initial encounters. ☐ Assure that treatment for LTBI is started for adult high- and medium-priority contacts without high-risk factors within 10 business days of their medical evaluations ☐ Review and assess the timeliness of initiating the treatment plans for contacts within 10 business days after their medical evaluations ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf Targeted Tuberculin Testing and Treatment of LTBI • www.cdc.gov/mmwr/PDF/rr/rr4906.pdf • Roadmap (**8.11**) • Protocols and Standing Orders (SHD) **Forms:** • Contact Investigation • Instructions

Tasks for Contact Investigation	Instructions and Forms
Review data and documentation weekly throughout the contact investigation: ☐ Reassess information about the index patient at least weekly until drug susceptibility results are available for the *Mycobacterium tuberculosis* isolate or for 2 months following notification, whichever is longer ☐ Review documentation to ensure that the contact list is complete ☐ Collect and analyze data on contacts and TST or IGRA tests ☐ Reassess contact priorities ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions
Report on the contact investigation: ☐ Report results of the initial TST/IGRA testing to the WA State TB Services after the initial testing is completed ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions

Monitor contacts on treatment for LTBI:
☐ Assure that contacts are assessed at least monthly for
  • Clinical follow-up
  • Adherence to LTBI treatment
  • Adverse reactions to LTBI treatment
	Instructions:
	• Roadmap (**8.11**)

Retest contacts: ☐ On contacts whose results were initially negative, repeat tuberculin skin testing/IGRA 8 to 10 weeks after each contact's last exposure to the index patient during the infectious period ☐ After retesting, reevaluate contacts who were initially TST- or IGRA - negative and started on LTBI treatment to determine if treatment should be continued ☐ After retesting, determine if transmission occurred and whether to expand the investigation ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) Contact Investigation Guidelines • www.cdc.gov/mmwr/pdf/rr/rr5415.pdf **Forms:** • Contact Investigation • Instructions

Tasks for Contact Investigation	Instructions and Forms
Report on the contact investigation: ☐ Report results of the second round of testing to the WA State TB Services after retests are completed ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions

Confirm contacts' completion of treatment for LTBI:
☐ Verify completion of treatment 6 to 12 months after treatment was started depending upon
  • Regimen
  • Adherence
  • Number of weeks on treatment
  • Number of doses taken
  • Chest radiograph	

Report on the contact investigation: ☐ Report completion of treatment to the WA State TB Services after contacts complete treatment for LTBI ☐ Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks	**Instructions:** • Roadmap (**8.11**) **Forms:** • Contact Investigation • Instructions

Introduction

Purpose

A contact investigation is the process of identifying, examining, evaluating, and treating all persons who are at risk for infection with *Mycobacterium tuberculosis* due to recent exposure to a newly diagnosed or suspected case of pulmonary, laryngeal, or pleural tuberculosis (TB).

The primary goal of a contact investigation is to do the following:

- Identify persons who were exposed to an infectious case of TB
- Ensure that contacts receive
  - Testing for *M. tuberculosis* infection;
  - Screening for TB disease;
  - Medical evaluation, if indicated;
  - Prompt initiation of treatment for latent tuberculosis infection (LTBI) if at high risk for developing TB disease (younger than 5 years of age or immunocompromised); and
  - A complete, standard course of treatment, unless medically contraindicated.[1]

Secondary goals of a contact investigation are to

- Stop transmission of *M. tuberculosis* by identifying persons with previously undetected infectious TB; and
- Determine whether a TB outbreak has occurred (in which case, an expanded outbreak investigation should ensue).[2]

Use this section to understand and follow national and Washington State guidelines to address the following:

- Decide when to initiate a contact investigation
- Understand the time frames for key contact investigation activities
- Estimate the infectious period
- Conduct index patient interviews
- Assign priorities to contacts
- Complete contact evaluation, treatment, and follow-up
- Determine when to expand a contact investigation
- Manage data and evaluate contact investigations
- Conduct an outbreak investigation

Except in rare cases, every case of TB begins as a contact to a person with active pulmonary, laryngeal, or pleural TB disease. For this reason, the Centers for Disease Control and Prevention (CDC) has identified contact investigations (i.e., seeking and evaluating contacts) as a fundamental strategy for the prevention and control of TB. To control and prevent TB, our healthcare resources and efforts in Washington State should be directed to meeting the priorities outlined in the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America." One of the recommended strategies for achieving the goal of reduction of TB morbidity and mortality is prompt identification of contacts to patients with infectious TB and timely treatment of those at risk with an effective drug regimen.[3] National recommendations for contact investigations are provided in the CDC's "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC, and Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States" (*MMWR* 2005;54[No. RR-15]:1–49).

One of the major challenges to successful control of TB is preventing development of TB disease in contacts of persons with infectious TB and in preventing and responding to TB outbreaks.[4] Reducing the risk of TB among contacts through the development of better methods of identification, evaluation, and management would lead to substantial personal and public health benefits and facilitate progress toward eliminating TB in the United States.[5]

The evaluation of contacts of cases of infectious TB is one of the most productive methods of identifying adults and children with LTBI at high risk for progression to TB disease and persons already in the early stages of TB disease. Contact investigations, therefore, serve as an important means of detecting TB cases and, at the same time, identify persons in the early stage of LTBI, when the risk for progression to TB disease is high and the benefit of treatment is greatest.

Policy

A contact investigation is recommended for the following forms of suspected or confirmed TB because they are likely to be infectious:

Pulmonary, laryngeal, or pleuropulmonary disease with either:

- Pulmonary cavities or
- Respiratory specimens that have acid-fast bacilli (AFB) on microscopy or
- (Especially) both.[6]

Persons with AFB sputum smear negative results are less likely to be infectious, but are still capable of infecting others.

Structure of a Contact Investigation

Basic Steps of a Contact Investigation

A successful contact investigation requires the careful gathering and evaluation of detailed information, often involving many people. In general, contact investigations follow a process that includes these steps:

1. Preinterview preparation
2. Index patient interviews
3. Field investigation
4. Risk assessment for *Mycobacterium tuberculosis* transmission
5. Decision about priority of contacts
6. Evaluation of contacts
7. Treatment and follow-up of contacts
8. Decision about whether to expand testing
9. Evaluation of contact investigation activities[7,8]

Although these steps are presented in sequence above, it is important to remember that contact investigations do not always follow a predetermined sequence of events.[9]

Contact Investigation Plan

The investigation plan starts with information gathered during interviews and site visits. It should include a registry of the contacts, their assigned priorities, and a written timeline. The timeline sets expectations for monitoring the progress of the investigation, and it assists the local health jurisdiction TB Services staff in informing public health officials about whether additional resources are needed for finding, evaluating, and treating the high- and medium-priority contacts.

The plan is a work in progress and should be revised if additional information indicates a need to expand a contact investigation. It is part of the permanent record of the overall investigation available for later review and program evaluation.

"Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Decision to Initiate a Contact Investigation

Factors Predicting Transmission of Tuberculosis

Decide when to initiate a contact investigation using the criteria provided in this topic. Competing demands restrict the resources that can be allocated to contact investigations. Therefore, local health jurisdiction personnel must decide which contact investigations are more significant and which contacts to evaluate first.

The index patient is the first patient that comes to the investigator's attention as an indicator of a potential public health problem. Whether or not to investigate an index patient depends upon factors predicting transmission. See Table 1: Index Patient Factors Increasing Transmission Risk**.** In addition, other information about the index patient, such as social habits or workplace environments, can influence the investigative strategy.[10]

TABLE 1: INDEX PATIENT FACTORS INCREASING TRANSMISSION RISK [11]

Characteristics of the Index Patient	Behaviors of the Index Patient
• Pulmonary, laryngeal, or pleuropulmonary tuberculosis (TB) • Positive acid-fast bacilli sputum smear results • Cavitation on chest radiograph • Adolescent or adult patient • Lack of treatment or ineffective treatment of TB disease	• Frequent coughing • Sneezing • Singing • Close social network

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54 (No. RR-15):4.

Anatomical Site of Disease

Ordinarily, patients with pulmonary or laryngeal tuberculosis (TB) are the only ones who can transmit infection. For contact investigation purposes, pleural disease is grouped with pulmonary disease because sputum cultures can yield *Mycobacterium tuberculosis* even when no lung abnormalities show on radiography. Rarely, extrapulmonary TB causes transmission during medical procedures, such as autopsy and embalming, that release aerosols.

Sputum Bacteriology

The relative infectiousness increases when the sputum culture results are positive, and increases further when the acid-fast bacilli (AFB) sputum smear results are also positive.[12] The significance of results from respiratory specimens other than expectorated sputum, such as bronchial washings or bronchoalveolar lavage fluid, is undetermined. Expert opinion recommends that these specimens be regarded as equivalent to sputum.

Radiographic Findings

Patients who have lung cavities observed on a chest radiograph are more infectious than patients with noncavitary disease. This is an independent predictor after bacteriologic findings are taken into account. The significance of small lung cavities that are detectable with computerized tomography (CT), but not with plain radiography, is undetermined.

Isolated instances of highly contagious endobroncheal TB in severely immunocompromised patients who temporarily had normal chest radiographs have contributed to outbreaks. The number and relative significance of such instances is unknown, but in one case series with human immunodeficiency virus (HIV)-infected TB patients, 3% who had positive AFB sputum smears had normal chest radiographs at the time of diagnosis.

Social Characteristics

Social issues can influence transmission. To assess the risk of transmission, it is important to consider the index patient's social factors, such as a close social network, residential setting or homelessness, employment, work setting, non-work-related activities, recent arrival from a foreign country, substance abuse and intravenous drug use.

Age

Transmission from children younger than 10 years of age is unusual, although it has been reported in association with those pulmonary forms of disease typically seen in adults. Contact investigations to evaluate transmission from pediatric cases should not be undertaken, except for those unusual cases. However, children younger than 5 years with TB, regardless of the site of disease, should have a contact investigation to identify the source case. A source-case investigation seeks the source of recent *M. tuberculosis* infection, perhaps newly diagnosed TB disease. TB disease in children younger than 5 years typically indicates that the infection is recent. Young children usually do not transmit TB to others, and their contacts are unlikely to be infected because of exposure to them.

Human Immunodeficiency Virus Status

Evaluation of HIV status must be performed promptly since progression to active TB may occur within weeks of exposure among individuals with acquired immunodeficiency syndrome (AIDS). HIV-infected TB patients with low CD4 T-cell counts frequently have chest radiographic findings that are not typical of pulmonary TB.[13] In particular, they are more likely to have mediastinal adenopathy and less likely to have upper-lobe infiltrates and cavities. The atypical radiographic findings increase the potential for delayed diagnosis, which increases transmission. However, HIV-infected patients who have pulmonary or laryngeal TB on average are only as contagious as similar patients who are not HIV infected. Contacts to HIV-infected index TB cases are also more likely to be HIV infected. Therefore, for all persons who were exposed to HIV-infected TB cases (or those with risk factors for HIV) and whose infection status is unknown, HIV counseling and testing is recommended.[14] Regardless of known HIV status, HIV counseling and testing should be recommended for all patients as a part of the screening process.[15]

After Starting Chemotherapy

TB patients rapidly become less contagious while under treatment. This has been corroborated by measuring the number of viable *M. tuberculosis* organisms in sputum samples and by observing infection rates in household contacts. However, the exact amount of time it takes for an individual patient to be non-infectious cannot be accurately predicted. Therefore, each patient's situation must be evaluated according to their sputum sample results, response to therapy and results of contact investigation. .

Treatment After Exposure to Drug-Resistant Tuberculosis

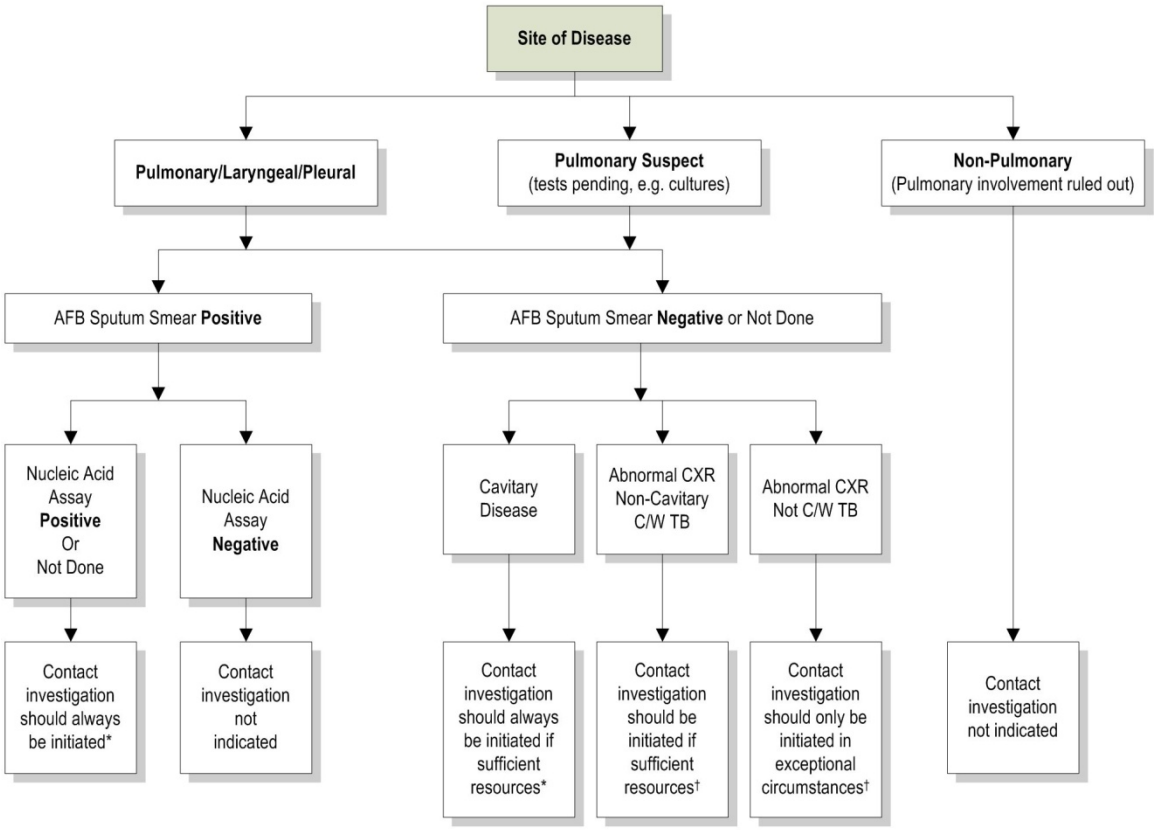
Drug susceptibility results for the *M. tuberculosis* isolate from the index patient (i.e., the presumed source of infection) are absolutely necessary for selecting the treatment regimen.

Resistance to isoniazid (INH) alone leaves the option of preventive treatment of contacts with four months of daily rifampin (RIF), but resistance to both INH and rifampin constitutes multidrug-resistant TB (MDR-TB). Treatment by all potential regimens is poorly tolerated to some extent, while none of these regimens have been tested fully for efficacy. Therefore, a consultation with a physician having expertise in this area is strongly recommended for selecting a regimen and managing the care of contacts. Monitor contacts who are suspected to be infected with multidrug-resistant *M. tuberculosis* for two years after exposure.

Deciding to Initiate a Contact Investigation

Consider a contact investigation for any patient with confirmed or suspected pulmonary, laryngeal, or pleuropulmonary TB. Refer to Figure 1 to help determine whether to start a contact investigation.

FIGURE 1: DECISION TO INITIATE A CONTACT INVESTIGATION[16]



Definitions of abbreviations: AFB = acid-fast bacilli; C/W = consistent with; CXR = chest radiograph; TB = tuberculosis.
* Use time frames from the middle column of Table 2 in the "Time Frames for Contact Investigation" topic.
† Use time frames from the right-hand column of Table 2 in the "Time Frames for Contact Investigation" topic.
Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):5.

In general, a contact investigation should be promptly initiated for an AFB sputum smear-positive pulmonary, laryngeal or pleural TB suspect. Although sputum smear-positive suspects may eventually prove to have nontuberculous mycobacteria, (NTM) rather than. *M. tuberculosis,* opportunities for appropriate contact investigation may be delayed, or even lost, if the TB program is waiting for confirmation of TB disease by positive culture.

If AFB are not detected by microscopy of three sputum smears, an investigation is still recommended if the chest radiograph shows cavities in the lung. Small parenchymal cavities that can be detected only by computerized imaging techniques (e.g., computed tomography [CT], computerized axial tomography [CAT] scan, or magnetic resonance imaging [MRI] of the chest) are not considered to be "cavitary disease."

When sputum samples have not been collected, either because of an oversight or the patient's inability to produce sputum samples, results from other types of respiratory specimens (e.g., gastric aspirates or bronchoalveolar lavage) may be interpreted in the same way as in the above recommendations. However, whenever feasible, sputum samples for each case should be collected before or while initiating chemotherapy.

For patients whose samples were reported to be positive on smear or culture at other laboratories, local health jurisdictions (LHJ) should consider collection and submission of sputum specimens on TB suspects to the Washington State Department of Health Public Health Laboratory. Doing so facilitates more rapid completion of testing and reporting to the LHJ. In addition, this provides an isolate to be sent automatically for universal genotyping.

For information regarding submission of sputum specimens to the Washington State Department of Health Public Health Laboratory, refer to the "Specimen Collection" topic in the Laboratory Services Section of the manual (**10.13**)

A contact investigation may still be considered for high-risk contacts of suspects with non-cavitary disease and negative AFB sputum smears. The decision depends on the amount of resources that can be allocated and on whether goals are being met for higher priority contact investigations.

Contact investigations generally should not be initiated around index patients who have suspected TB disease and minimal diagnostic findings in support of pulmonary TB**.** Possible exceptions can be found during outbreak investigations, especially when vulnerable or susceptible contacts are found, or during a source-case investigation. Outbreak investigations and source-case investigations are explained briefly below.

- **Outbreak Investigation:** Definitions for TB outbreaks are relative to the local context. Outbreak cases can be distinguished from other cases only when some association in time, location, patient characteristics, or *M. tuberculosis* attributes (e.g., drug resistance or genotype) becomes apparent. In low-incidence jurisdictions, any temporal cluster will cause suspicion regarding an outbreak. In places where cases are more common, clusters can be obscured by the baseline incidence rate until suspicion is triggered by a noticeable increase, a sentinel event (e.g., pediatric cases), or related *M. tuberculosis* isolates.

- **Source-Case Investigation:** A source-case investigation seeks the source of recent *M. tuberculosis* infection, perhaps newly diagnosed TB disease. A source case or patient is the original source of infection for secondary cases or contacts. The source case can be, but is not necessarily, the index patient.

For more information on source-case investigations, see the CDC's "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis Cases" (*MMWR* 2005;54[No. RR-15]: 31) at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Time Frames for Contact Investigation

Use this topic to understand the time frames for key contact investigation activities. A suspected or confirmed case of tuberculosis (TB) becomes designated as an “index patient” when that person is the first patient to appear as an indicator of a potential public health problem. An investigation is launched because of an index patient and the investigation often starts with an interview of the index patient.

Information about the Index Patient and Transmission Sites

Comprehensive information about an index patient is the foundation of a contact investigation. This information includes the disease characteristics, the onset date of the illness, names of contacts, exposure locations, and current medical factors, such as initiation of effective treatment and drug susceptibility results.

The infectiousness of the index patient determines the recommended time frames for pursuing the investigation. Indications of infectiousness include symptoms (such as cough, fever, weight loss, and night sweats), a positive acid-fast bacilli (AFB) sputum smear, a positive nucleic acid amplification (NAA) test, cavitary disease, or an abnormal chest radiograph consistent with TB.

Refer to Table 2: Time Frames for Investigating the Index Patient and the Sites of Transmission for the recommended time frames for index patient interviews and visits to the residence or other transmission sites, or see the CDC’s “Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis” at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

Some readers confuse prioritizing an investigation with prioritizing follow-up of individual contacts within an investigation. The following explains the difference between the two:

- The time priority for investigating the index patient and transmission sites is determined by the infectiousness of the index patient. Indications of infectiousness include positive AFB sputum smear results as well as symptoms, positive NAA test results, and chest radiographs showing cavitary disease or abnormalities consistent with TB.
- Ranking contacts by priority for follow-up within an investigation is based upon the characteristics of the index patient as well as the duration and circumstances of the exposure, and the vulnerability/susceptibility of the contacts to progression from TB infection to development of TB disease (such as contacts under 5 years of age or with HIV infection, immunosuppression, underlying disease processes).

TABLE 2: TIME FRAMES FOR INVESTIGATING THE INDEX PATIENT AND THE SITES OF TRANSMISSION[17]

Activity	Suspects Expected to Be Cases of Tuberculosis (TB)	
	Suspects with Indications of Infectiousness	Suspects Without Indications of Infectiousness
First Index Patient Interview Number of days following notification within which the index patient should be interviewed in person (i.e., not by telephone)	**≤1 Business Day of Reporting**	**≤3 Business Days of Reporting**
Residence Visit Number of days following the first index patient interview within which the place of residence of the index patient should be visited	**≤3 Business Days After First Interview**	**3 Business Days After First Interview**
Field Investigation Number of days following initiation of the contact investigation within which all potential settings for transmission should be visited	**5 Business Days After the Start of the Investigation**	**5 Business Days After the Start of the Investigation**
Index Patient Reinterviews Length of time after the first interview within which the index patient should be reinterviewed one or more times for clarification and additional information	**1 or 2 Weeks After First Interview**	**1 or 2 Weeks After First Interview**
Reassessment of Index Patient Information about the index patient should be reassessed at least weekly until drug-susceptibility results are available for the *Mycobacterium tuberculosis* isolate or for 2 months following notification, whichever is longer.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):7–8.

Contact Evaluation and Treatment

In addition to the investigation of the index patient and transmission sites, a contact investigation also involves contact follow-up. Refer to Table 3: Time Frames for Contact Evaluation and Treatment to monitor the progress of the investigation and determine whether additional resources are needed for finding, evaluating, and treating the high- and medium-priority contacts.

Priority-ranking contacts for investigation are based upon the likelihood of infection and the potential hazard to the individual contact if infected.[18] For information on how to determine which contacts are high-, medium-, or low-priority, see the Tuberculosis Contact Investigation Form, and Tuberculosis Contact Investigation Form Instructions.

CDC recommends that IGRA testing may be used in all circumstances in which the tuberculin skin test (TST) is currently used, including contact investigation.[19]

TABLE 3: TIME FRAMES FOR CONTACT EVALUATION AND TREATMENT[20]

Type of Contact	Business Days from Listing of a Contact to Initial Encounter*	Business Days from Initial Encounter to Completion of Medical Evaluation†	Business Days from Completion of Medical Evaluation to Start of Treatment
High-Priority Contact Index patient with positive acid-fast bacilli (AFB) sputum smear results or cavitary disease on chest radiograph	**3 Business Days After Being Listed in the Investigation[21]**	**5 Business Days**	**10 Business Days**
		5 Business Days Children and high-risk contacts can develop complicated tuberculosis (TB) within a few weeks of infection.	
High-Priority Contact Index patient with negative AFB sputum smear results	**3 Business Days After Being Listed in the Investigation[22]**	**10 Business Days**	**10 Business Days**
Medium-Priority Contact Regardless of AFB sputum smear or culture result	**3 Business Days After Being Listed in the Investigation[23]**	**10 Business Days**	**10 Business Days**

* "Encounter" means a face-to-face meeting, which gives the public health worker a chance to determine whether the contact is generally healthy or ill. The initial encounter also provides opportunities to administer a tuberculin skin test (TST) and to schedule further evaluation.

† The medical evaluation is complete when the contact's status relative to *Mycobacterium tuberculosis* infection or TB disease has been determined. A normal exception to this schedule is the delay in waiting for final mycobacteriology results, but this applies to relatively few contacts.

Source: Adapted from CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):9.

Ongoing Management Activities

Ongoing contact follow-up includes testing, medical evaluation, and treatment. Information from contact follow-up guides decisions about whether to expand a contact investigation. Refer to Table 4: Overview of Ongoing Management Activities and Maximum Time Frames to monitor the progress of ongoing contact follow-up and to determine if/when to expand the investigation.

TABLE 4: OVERVIEW OF ONGOING MANAGEMENT ACTIVITIES AND MAXIMUM TIME FRAMES[24]

Activity	Purpose	Maximum Time Interval
Review all documentation	To ensure that contact list is complete	Ongoing
Review and assess completeness of each contact's medical follow-up and treatment plan	To ensure appropriate and complete medical follow-up	5 business days after each contact's medical evaluation is completed*
Review and assess the timeliness of initiating the treatment plan	To avoid delays in treatment initiation, particularly in high-risk contacts	10 business days after each contact's medical evaluation is completed*
Determine if transmission occurred	To decide whether to expand investigation	At completion of follow-up testing, or if secondary cases are identified
Obtain and review drug-susceptibility results	To determine if contacts are receiving appropriate treatment for latent tuberculosis infection (LTBI)	1 to 2 months after the index patient's initial sputum collection date
Repeat tuberculin skin test (TST) or IGRA if contact is initially TST or IGRA -negative	To determine if contact has converted (TB Class I to TB Class II)	8 to 10 weeks after each contact's initial TST or IGRA or last exposure to the index patient†
Reevaluate contacts who were initially TST- or IGRA negative and started on LTBI treatment (Window Period Treatment for a TB Class I Contact)	To determine if treatment for LTBI should be continued	8 to 10 weeks after each contact's initial TST or IGRA or last exposure to the index patient before the end of the infectious period†
Assess contacts' adherence with medical follow-up and TB medication	To remove barriers and ensure timely and complete evaluation and follow-up	Monthly, at time of each visit
Ensure contacts are monitored for adverse reactions and toxicity of LTBI treatment regimens	To prevent development of adverse effects and toxicity from drug regimens	At least monthly while on LTBI treatment

Activity	Purpose	Maximum Time Interval
Evaluate problems and concerns that arise and may delay or hamper contact investigation	To remove barriers and ensure timely and complete evaluation and follow-up	Whenever problems are identified
Collect and analyze data to evaluate the contact investigation and complete the "TB Contact Investigation Summary" form for the WA State TB Services	To provide epidemiologic analysis of investigations and to measure performance using indicators that reflect performance objectives[25]	Ongoing

* The medical evaluation is complete when the contact's status relative to *Mycobacterium tuberculosis* infection or TB disease has been determined. A normal exception to this schedule is the delay in waiting for final mycobacteriology results, but this applies to relatively few contacts.

† Third TST/IGRA: In rare circumstances, an infectious index patient with advanced disease can stay infectious for several months. In these circumstances, the second TST/IGRA for negative contacts should be performed in the usual time frame (8 to 10 weeks). This will identify any contacts who have already converted so they can be evaluated for treatment. However, any household members who remain TST/IGRA negative and have continued exposure to the infectious index patient should have a third TST/IGRA 8 to 10 weeks after the index patient becomes noninfectious. This is especially true for contacts who are infants in a household where a resident is culture positive after 3 months or has multidrug-resistant TB. For example, a household member with continued exposure to an infectious index patient had a negative second TST/IGRA on 3/12/2007. The last date the index patient was infectious was 3/5/2007. The household member should have a third TST/IGRA 8 to 10 weeks from 3/5/2007

Source: Adapted from: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). Contact investigation guidelines. *CDHS/CTCA Joint Guidelines* [CTCA Web site]. November 12, 1998:18. Available at: http://www.ctca.org/fileLibrary/file_46.pdf

Infectious Period

Determine the infectious period to focus the investigation on those contacts most likely to be at risk for infection and to set the time frame for testing contacts.

The infectious period is the time frame in which potential exposure to others may have occurred while the patient was infectious or able to transmit tuberculosis (TB).[26] The exact start of the infectious period cannot be determined with any current methods, so a practical estimation is necessary. From expert opinion, an assigned start **3 months prior to TB diagnosis or onset of symptoms** is recommended for the more infectious patients. Some circumstances may indicate an even earlier start which should be used instead. The clearest example is when the patient or the patient's associates were aware of protracted illness, which can exceed one year in extreme examples.

Assemble information from the index patient interview and other sources to estimate the infectious period. Helpful details include the approximate dates that TB symptoms were noticed, bacteriology results, and the extent of disease, especially the presence of large lung cavities, which implies prolonged illness as well as increased infectiousness.

Use Table 5 to determine the start of the infectious period.

TABLE 5: GUIDE FOR ESTIMATING THE BEGINNING OF THE PERIOD OF INFECTIOUSNESS[27]

Index Patient Characteristics						
Tuberculosis Symptoms		Positive Acid-Fast Bacilli Sputum Smear Results		Cavitary Chest Radiograph		Recommended Beginning of Likely Period of Infectiousness
Yes	No	Yes	No	Yes	No	
✓			✓		✓	3 months prior to symptom onset or first positive finding consistent with tuberculosis (TB) disease (whichever is longer)
✓		✓		✓		3 months prior to symptom onset or first positive finding consistent with TB disease (whichever is longer)
	✓		✓		✓	4 weeks prior to date of suspected diagnosis
	✓	✓		✓		3 months prior to first positive finding consistent with TB

Source: California Department of Health Services Tuberculosis Control Branch; California Tuberculosis Controllers Association. Contact investigation guidelines. Berkeley, CA: California Department of Health Services; 1998; in CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):7.

For purposes of contact investigation, the end of potential exposure to the infectious case determines the end of the infectious period. The potential for transmission is reduced by the initiation and duration of treatment, the index patient's response to treatment, and/or the application of effective infection control measures.

In general, **for the purposes of contact investigation**, the infectious period is closed when contacts are no longer exposed to the patient **OR** when **all three** of the following criteria are met:

1. The index patient is receiving effective treatment (as demonstrated by *Mycobacterium tuberculosis* susceptibility results) for at least two weeks.
2. The index patient has diminished symptoms.
3. The index patient exhibits mycobacteriologic response (e.g., decrease in grade of sputum smear positivity detected on sputum-smear microscopy).[28,29]

Take careful note of the following exceptions:

- **Multidrug-resistant TB (MDR-TB):** MDR-TB can extend infectiousness if the treatment regimen is ineffective.
- **Signs of infectiousness:** Any index patient with signs of extended infectiousness should be continually reassessed for recent contacts.
- **Susceptible contacts:** Apply more stringent criteria for setting the end of the infectious period if particularly susceptible contacts are involved. (HIV infection, child under 5 years of age, immunosuppression, underlying disease processes)

A patient with pulmonary or laryngeal TB returning to a congregate living setting or to any setting in which susceptible persons might be exposed should meet **both** of the following two criteria for noninfectiousness:

1. Have had three consecutive AFB-negative sputum smear results from specimens collected 8 to 24 hours apart, with at least one being an early morning specimen, and
2. Have been on antituberculosis therapy for at least 2 weeks

Index Patient Interviews

Conduct index patient interviews to set the direction for the contact investigation, identify contacts, provide opportunities for the patient to learn about tuberculosis (TB) and its control, and help the public health worker learn how to provide treatment and care specific to that patient.

In index patient interviews, gather information about the index patient's medical history, treatment needs, residence, transmission sites, dates and times at specific transmission sites, and contacts at specific sites. Use the information from these interviews to decide whether to start a contact investigation, establish its priority relative to other investigations, and determine the scope of the investigation.

There should be an initial interview and one or two reinterviews before discharge from the hospital, or within one to two weeks if the initial interview occurs in the home, to obtain further information and answer additional questions.[30]

TB Interviewing for Contact Investigation: A Practical Resource for the Healthcare Worker (New Jersey Medical School Global Tuberculosis Institute Web site; 2004) at http://www.umdnj.edu/ntbcweb/products/tbinterviewing.htm offers specific suggestions on how to prepare for and conduct the interviews.[31]

Record information regarding the index patient and contacts on the Contact Investigation Form (FORMS).

Preinterview Preparation

Gather information regarding the patient and the circumstances of the illness to prepare for the first interview.

Consult these sources:

- Current medical record
- Physician
- Laboratory, clinic or other reporting source
- Infection control nurse (if the patient is hospitalized)

General Guidelines for Interviewing an Index Patient

1. Discuss confidentiality and privacy in frank terms to help the patient decide how to share information, and revisit these topics several times during the interview to stress their importance. Emphasize confidentiality, but inform the patient that relevant information may need to be shared with other local health jurisdiction staff or other persons who may assist in congregate settings to most efficiently determine which contacts need to be evaluated. Inform the patient that it will be necessary for visits to be made at sites such as the home, workplace/school, or leisure establishments to assess the shared air environment and accurately structure the contact investigation.[32]
2. Conduct the interviews in the patient's language, using a medical interpreter if the patient does not speak English.
3. Conduct the interviews in a culturally competent manner.

For more information on cultural sensitivity, refer to the *Participant's Workbook* for Session 4: "Working with Culturally Diverse Populations" in the *Directly Observed Therapy Training Curriculum for TB Control Programs* (Curry International Tuberculosis Center Web site; 2003) at http://www.currytbcenter.ucsf.edu/catalogue/epub/index.cfm?tableName=DOTE

For assistance with language issues, see the *Language Services Resource Guide for Health Care Providers* (The National Health Law Program Web site; 2006) at http://www.healthlaw.org/images/pubs/ResourceGuideFinal.pdf

Field Investigation

A field investigation includes visiting the patient's home or shelter, workplace or school (if any), and the other places where the patient said he or she spent time while infectious. The field investigation is important and should be done even if the patient interview has already been conducted. The purpose of the field investigation is to identify contacts and evaluate the environmental characteristics of the place or places in which exposure may have occurred. The field investigation may provide additional information for use in the risk assessment and for identifying additional contacts.[33]

During field visits, the healthcare worker should do the following:

- **Observe environmental characteristics**, such as room size, crowding, and ventilation, to estimate the risk of tuberculosis (TB) transmission. Air volume, exhaust rate, and circulation assist in predicting the likelihood of transmission in an enclosed space. In large indoor settings, the degree of proximity between contacts and the index patient can influence the likelihood of transmission. The most practical system for grading exposure settings is to categorize them by size (e.g., “1” being the size of a vehicle or car, “2” the size of a bedroom, “3” the size of a house, and “4” a size larger than a house). The volume of air shared between an infectious TB patient and contacts dilutes the infectious particles. Local circulation and overall room ventilation also dilute infectious particles, but both factors have to be considered because they can redirect exposure into spaces that were not visited by the index patient.[34]
- **Identify additional contacts** (especially children) and their locating information, such as phone numbers and addresses.
- **Look for evidence of other contacts** who may not be present at the time of the visit (for example, pictures of others who may live in or visit the house, shoes of others who may live in the house, or toys left by children).
- **Interview and apply skin tests (TST’s) or draw blood for IGRA testing on high- and medium-priority contacts** who are present and arrange for reading of the Tuberculin Skin Test (TST) results.
- **Educate the contacts** about the purpose of the contact investigation, the basics of transmission, the risk of transmitting *Mycobacterium tuberculosis* to others, and the importance of testing, treatment, and follow-up for TB infection and disease.
- **Refer contacts who have TB symptoms** to the local health jurisdiction or a community based healthcare provider for a medical evaluation, including radiography and sputum collection.[35]

Healthcare workers should remember to follow infection control precautions while visiting a potentially infectious TB patient at home or in any other location. These precautions may include wearing a personal respirator.[36]

For more information on infection control, "Guidelines for Isolation Precaution" at http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html and "Guidelines for Preventing the Transmission of Mycobacterium Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

Another critical consideration during field investigations is safety. Healthcare workers should become familiar with policies and recommendations of local law enforcement agencies and local health jurisdiction administration policies regarding personal safety. Current information regarding local high-risk areas for crime can be very valuable in planning and conducting safe field visits.

General safety precautions that are recommended for the healthcare worker include the following:

- Wearing an identification badge with a current photo
- Working in pairs when visiting a potentially dangerous area
- Informing your supervisor or other coworkers of your itinerary and expected time of return, especially if you anticipate problems[37]

Contact Priorities

Assign priorities to contacts, using the registry of contacts compiled from the index patient interviews, site visits, interviews with contacts, and information from other persons involved in the investigation. The Centers for Disease Control and Prevention (CDC) defines the three levels of contact priorities as follows:

- High-priority contacts
- Medium-priority contacts
- Low-priority contacts

Contact priorities are determined by the likelihood of infection and the potential hazards to the individual contact if infected.[38] Priority-ranking contacts for investigation is based upon the characteristics of the index patient, the duration and circumstances of the exposure, and the vulnerability/susceptibility of the contacts to disease from *Mycobacterium tuberculosis* infection.[39]

Use the assigned priorities to allocate resources to complete all investigative steps for the high- and medium-priority contacts.[40] Dividing contacts into these three levels provides a system for public health staff to reach high-priority contacts first, then medium- and low-priority contacts. The priority scheme directs resources to the following essential actions:

1. Find contacts who are secondary active tuberculosis (TB) cases.
2. Find contacts who have recently acquired *M. tuberculosis* infection—the most likely to benefit from treatment.
3. Select contacts who are most likely to progress to TB disease if they are infected (i.e., susceptible contacts) or who could suffer severe morbidity if they develop TB disease (i.e., vulnerable contacts).[41] (These include contacts under 5 years of age or with HIV infection, immunosuppression, underlying disease processes.)

For more information see the CDC's "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Index Patient with Positive Acid-Fast Bacilli Sputum Smear Results or Cavitary Tuberculosis

Use Table 6 to prioritize contacts to index cases with sputum smear-positive or cavitary disease.

TABLE 6: PRIORITIZATION OF CONTACTS TO SMEAR-POSITIVE OR CAVITARY CASES[42]

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
• Household contacts • Contacts <5 years old • Contacts with human immunodeficiency virus (HIV) infection or other immunocompromising condition • Contacts with exposure during a medical procedure such as bronchoscopy, sputum induction, or autopsy • Contacts with exposure in a congregate setting • Contacts whose exposure occurs in poorly ventilated areas and for significant periods of time*	• Contacts not in high-priority groups • Contacts 5–15 years old • Contacts whose exposure occurs in poorly ventilated areas and for significant periods of time*	• Contacts not in high-priority groups • Contacts not in medium-priority groups

* Observe environmental characteristics, such as room size, crowding, and ventilation, to estimate the risk of tuberculosis (TB) transmission: air volume, exhaust rate, and circulation predict the likelihood of transmission in an enclosed space. In large indoor settings, the degree of proximity between contacts and the index patient can influence the likelihood of transmission. The most practical system for grading exposure settings is to categorize them by size (e.g., "1" being the size of a vehicle or car, "2" the size of a bedroom, "3" the size of a house, and "4" a size larger than a house). The volume of air shared between an infectious TB patient and contacts dilutes the infectious particles. Local circulation and overall room ventilation also dilute infectious particles, but both factors have to be considered because they can redirect exposure into spaces that were not visited by the index patient.[43]

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):12.

Index Patient with Negative Acid-Fast Bacilli Sputum Smear Results

Use Table 7 to prioritize contacts to index cases with sputum smear-negative results

TABLE 7: PRIORITIZATION OF CONTACTS TO SMEAR-NEGATIVE CASES[44]

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
• Contacts <5 years old • Contacts with human immunodeficiency virus (HIV) infection or other immunocompromising conditions • Contacts exposed during a medical procedure, such as bronchoscopy, sputum induction, or autopsy	• Contacts not in high-priority groups • Household contacts • Contacts exposed in a congregate setting • Contacts whose exposure occurs in poorly ventilated areas and for significant periods of time*	• Contacts not in high-priority groups • Contacts not in medium-priority groups
* Observe environmental characteristics, such as room size, crowding, and ventilation, to estimate the risk of tuberculosis (TB) transmission: air volume, exhaust rate, and circulation predict the likelihood of transmission in an enclosed space. In large indoor settings, the degree of proximity between contacts and the index patient can influence the likelihood of transmission. The most practical system for grading exposure settings is to categorize them by size (e.g., "1" being the size of a vehicle or car, "2" the size of a bedroom, "3" the size of a house, and "4" a size larger than a house). The volume of air shared between an infectious TB patient and contacts dilutes the infectious particles. Local circulation and overall room ventilation also dilute infectious particles, but both factors have to be considered because they can redirect exposure into spaces that were not visited by the index patient.[45]		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):13.

Index Patient with Negative Bacteriologic Results and Abnormal Chest Radiographs Not Consistent with Tuberculosis

Use Table 8 to prioritize contacts to a suspected case of pulmonary TB who is acid-fast bacilli (AFB) sputum smear negative, nucleic acid amplification (NAA) negative, and culture negative, and who has abnormal chest radiographs not consistent with TB disease.

TABLE 8: PRIORITIZATION OF CONTACTS TO CASES WITH NEGATIVE BACTERIOLOGIC RESULTS AND ABNORMAL CHEST RADIOGRAPHS NOT CONSISTENT WITH TUBERCULOSIS[46]

High-Priority Contacts	Medium-Priority Contacts	Low-Priority Contacts
	• Household contacts • Contacts <5 years old • Contacts with human immunodeficiency virus (HIV) infection or other medical risk factor • Contacts exposed during a medical procedure, such as bronchoscopy, sputum induction, or autopsy	• Contacts not in medium-priority groups

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):14.

Contact Evaluation, Treatment, and Follow-up

Complete evaluation, treatment, and follow-up for high- and medium-priority contacts, as specified in your contact investigation plan. The Centers for Disease Control and Prevention (CDC) recommends the following:

- Provide each high- and medium-priority contact an initial assessment that includes a face-to-face encounter in which an impression of each contact's general health is formed and a tuberculin skin test (TST) is administered or blood is drawn for interferon gamma release assay (IGRA).
- Medically evaluate each high- and medium-priority contact to determine whether tuberculosis (TB) disease or latent tuberculosis infection (LTBI) are present or absent.
- Timely initiation of treatment is especially important for high-priority contacts and for contacts likely to progress to TB disease if they are infected (i.e., susceptible contacts) or contacts who could suffer severe morbidity if they had TB disease (i.e., vulnerable contacts, including those under 5 years of age or with HIV infection, immunosuppression, or underlying disease processes).
- Use the same diagnostic methods for all contacts, except when they have medical or constitutional conditions making TB more likely or more difficult to diagnose. A contact's country of origin and bacille Calmette-Guérin (BCG) vaccination (*See note below*) are not included in algorithms for diagnosis or treatment. Interpret a positive TST in a foreign-born or BCG-vaccinated person as evidence of recent *Mycobacterium tuberculosis* infection in contacts of persons with infectious cases. Evaluate these contacts for TB disease and offer them a course of treatment for LTBI.[47]

IGRA testing results are not affected by BCG vaccination, so its use is especially encouraged when tuberculin skin test (TST) results may be in question.

Forms

- Contact Investigation Form
- Form Instructions

Imunocompromised Contacts and Children under 5

Use Table 9 to select evaluation, treatment, and follow-up activities for contacts who are immunocompromised and/or under 5 years old.

Evaluate contacts who are immunocompromised or under 5 years of age with medical history, physical examination, chest radiograph, and tuberculin skin test (TST) or IGRA. Based upon the results of these evaluations, follow the action steps outlined in Table 9.

TABLE 9: EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPROMISED CONTACTS AND CHILDREN UNDER 5 YEARS OLD[48]

If evaluation or test results show that a contact has		Then take this action or these actions
Symptoms consistent with TB disease and/or Abnormal chest radiograph		Fully evaluate for TB disease
No symptoms consistent with TB disease and normal chest radiographs	1st TST* ≥5 mm or IGRA positive	Complete a full course of treatment for LTBI
	1st TST <5 mm or IGRA negative **and** ≥8 weeks since last exposure	• If not HIV-infected, no further evaluation required • If HIV-infected, no further evaluation required; consider a full course of treatment for LTBI
	1st TST <5 mm or IGRA negative **and** <8 weeks since last exposure	Begin treatment for LTBI and retest 8–10 weeks post exposure
	2nd TST ≥5 mm or IGRA positive	Complete a full course of treatment for LTBI
	2nd TST <5 mm or IGRA negative	• If not HIV-infected, no further evaluation required • If HIV-infected, no further evaluation required; consider a full course of treatment for LTBI

Definitions of abbreviations: HIV = human immunodeficiency virus; IGRA=Interferon Gamma Release Assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.
* **Note:** An IGRA test may be used in place of a TST.

*Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):15–16.

Immunocompetent Adults and Children 5 and Older (High- and Medium-Priority Contacts)

Use Table 10 to select evaluation, treatment, and follow-up activities for high- and medium-priority contacts who are immunocompetent and/or 5 years of age or older. Evaluate these contacts with medical history, exposure history, and TST or IGRA. Based upon the results of these evaluations, follow the action steps outlined in Table 10.

TABLE 10: EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPETENT ADULTS AND CHILDREN 5 YEARS AND OLDER (HIGH-AND MEDIUM-PRIORITY CONTACTS)[49]

If evaluation or test results show that a contact has		Then take this action or these actions
Symptoms consistent with TB disease		Fully evaluate for TB disease
No symptoms consistent with TB disease	1st TST* ≥5 mm or IGRA negative	Evaluate with a physical examination and CXR: • If CXR abnormal, fully evaluate for TB disease • If CXR normal, complete a full course of treatment for LTBI
No symptoms consistent with TB disease	1st TST <5 mm or IGRA negative **and** ≥8–10 weeks since last exposure	No further evaluation or treatment required
No symptoms consistent with TB disease	1st TST <5 mm or IGRA negative **and** <8 weeks since last exposure	Retest 8–10 weeks post exposure
No symptoms consistent with TB disease	2nd TST ≥5 mm or IGRA positive	Evaluate with a physical examination and CXR: • If CXR abnormal, fully evaluate for TB disease • If CXR normal, complete a full course of treatment for LTBI
No symptoms consistent with TB disease	2nd TST <5 mm or IGRA negative	No further evaluation or treatment required

Definitions of abbreviations: CXR = chest radiograph; IGRA=Interferon Gamma Release Assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.
* **Note:** An IGRA test may be used in place of a TST.

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):17.

Contacts with Prior Positive Tuberculin Skin Tests

Use Table 11 to select evaluation, treatment, and follow-up activities for contacts who have prior positive TSTs or IGRAs. Evaluate contacts with medical and exposure history. Based upon the results of these evaluations, follow the action steps outlined in Table 11.

TABLE 11: EVALUATION, TREATMENT, AND FOLLOW-UP OF CONTACTS WITH PRIOR POSITIVE TUBERCULIN SKIN TESTS[50]

If evaluation or test results show that a contact has		Then take this action or these actions
Symptoms consistent with TB disease		Fully evaluate for TB disease

No symptoms consistent with TB disease	Immunocompromised
	or
	<5 years old
		Evaluate with a physical examination and CXR:
		• If CXR or physical examination is indicative of TB disease, fully evaluate for TB disease
		• If results are **not** indicative of TB disease:
		  • If contact previously completed treatment, consider retreatment
		  • If treatment **not** completed previously, complete a full course of LTBI treatment

No symptoms consistent with TB disease	Immunocompetent and ≥5 years old	• If contact previously completed treatment for LTBI, no further evaluation or treatment required • If contact has **not** completed treatment for LTBI, consider treatment for LTBI
Definitions of abbreviations: CXR = chest radiograph; LTBI = latent tuberculosis infection; TB = tuberculosis.		

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):19.

When to Expand a Contact Investigation

Guidelines for Expanding an Investigation

Determine when to expand a contact investigation using the following guidelines:

1. Do not include lower-priority contacts unless objectives for high- and medium-priority contacts are being met.
2. Consider the extent of recent transmission.
3. Consider expanding the scope (e.g., number of contacts) of an investigation if any one or more of the following criteria are met:
   - **a.** Unexpectedly large rate of tuberculosis (TB) infection or disease in high-priority contacts, which is defined as 10% or at least twice the rate of a similar population without recent exposure, whichever is greater

     Since the background prevalence of tuberculosis infection in adult foreign-born populations from high-incidence countries often exceeds 30%, it is important to stratify the infection rates by country of birth and/or length of residence and by age. For example, in a community with a population comprised of large numbers of individuals born outside of the United States, the infection rate may exceed 30% in a contact investigation. In this case, separate U.S.-born individuals from foreign-born and determine the infection rate using the U.S.-born results.
   - **b.** Evidence of second-generation transmission (i.e., from TB patients who were infected after exposure to the source patient)
   - **c.** TB disease in any contacts who had been assigned low priority
   - **d.** Infection in any contacts younger than 5 years old
   - **e.** Contacts with a change in TST or IGRA status from negative to positive
4. When results from an investigation indicate that it should be expanded, but resources are insufficient, seek assistance from the next higher public health administrative level.

In general, without evidence of recent transmission, do not expand an investigation to lower-priority contacts. When program evaluation objectives have not been met, expand a contact investigation only in exceptional circumstances, generally involving highly infectious cases with high rates of infection among contacts or evidence for secondary cases and secondary transmission. Derive the strategy for expanding an investigation from the data obtained from the investigation to that point in time. Without data from the initial contact investigation to support evidence of transmission, there is little support to expand to lower-priority contacts. As in the initial investigation, review the incoming results of the expanded investigation at least weekly to reassess the strategy.

Low-Priority Contacts

Use Table 12 to select evaluation, treatment, and follow-up activities for low-priority contacts. Evaluate these contacts with medical and exposure history. Based upon the results of these evaluations, follow the action steps outlined in Table 12.

TABLE 12: EVALUATION, TREATMENT, AND FOLLOW-UP OF LOW-PRIORITY CONTACTS[51]

If evaluation or test results show that a contact has		Then take this action or these actions:
Symptoms consistent with TB disease		Fully evaluate for TB disease
No symptoms consistent with TB disease	8–10 weeks since last exposure	Evaluate with a TST or IGRA test
No symptoms consistent with TB disease	<8 weeks since last exposure	Wait 8–10 weeks after last exposure, and then evaluate with a TST or IGRA test
No symptoms consistent with TB disease	1st TST* ≥5 mm or IGRA positive	Evaluate with physical examination and CXR: • If CXR is abnormal, fully evaluate for TB disease • If CXR is normal, consider treatment for LTBI
No symptoms consistent with TB disease	1st TST <5 mm or IGRA negative	No further evaluation or treatment required

Definitions of abbreviations: CXR = chest radiograph; IGRA=Interferon Gamma Release Assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.
* **Note:** An IGRA may be used in place of a TST.

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):22.

Data Management and Evaluation of Contact Investigations

Data collection related to contact investigation has three broad purposes:

1. Management of care and follow-up of individual index patients and contacts
2. Epidemiological analysis of an investigation in progress as well as overall results of previous investigations
3. Program evaluation via performance indicators that reflect performance objectives

Reasons Contact Investigation Data Are Needed

Comprehensive Care

For each index patient and the associated contacts, a broad amount of demographic, epidemiological, historical, and medical information is needed for providing comprehensive care. The care for these individuals can extend to longer than a year in some instances, so the information builds stepwise and has numerous longitudinal elements (e.g., clinic visits attended, treatment doses administered and bacteriological response to treatment).

Timeline Objectives

Many of these data elements also contribute to the other reasons for collecting data. Data on some process steps are necessary for monitoring whether the contact investigation is keeping to the timeline objectives (e.g., how soon after listing is the TST or IGRA test obtained on a contact).

Completion of Investigation

When aggregated, the data from an investigation provides timeliness measures of initiation of investigation and evaluation of contacts. The analysis of data also contributes to reassessments of the strategy used in the investigation (e.g., was the infection rate greater for contacts believed to have more exposure?).

Reassessment of Strategy

The data from a completed investigation and all investigations in a fixed period (e.g., six months) show achievements in meeting program objectives, such as observance of timelines and completion of therapy for infected contacts. These core measurements for program evaluation, however, cannot directly show why objectives were not met. If the data are structured and stored in formats allowing detailed retrospective review, barriers may be identified and interventions recommended for future practice.

To assess the overall activities of contact investigation, see CDC's "Framework of Program Evaluation in Public Health" (*MMWR* 1999;48[No. RR-11]), at ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr4811.pdf.

Approach

Follow a systematic, consistent approach to data collection, organization, analysis, and dissemination.

1. Collect specific data elements on index patients and their contacts. The data elements should permit calculation of program performance indices.
2. Collect data on standardized (paper or electronic) forms.
3. Supply data definitions and formats for use by persons who collect, use, and interpret contact investigation data.
4. Whenever feasible, use data definitions and formats that are standard among jurisdictions.
5. Store data electronically for quick analysis of interim results.
6. Implement policies for data management that enable quick analysis of interim results.
7. Implement policies for data management and storage that specify the assignment of responsibilities.
8. Implement training and policies for data accuracy, completeness, and security.
9. Periodically summarize and review data during a particular contact investigation and for overall contact investigations.
10. Evaluate programs for contact investigation activities at least annually. Evaluation is an integral part of TB program responsibility.
11. Beyond standard data elements shown in these guidelines, collection and analysis of specific additional elements can contribute to local program management.

Index Patient and Contact Data

For data required on each index patient and contact, see Table 13 and Table 14.

TABLE 13: DATA ABOUT THE INDEX PATIENT[52]

Identifiers/Demographic Information	• Case manager • Name and aliases • For minors and dependents: guardian information • Date of birth • Social security number • Current locating information and emergency contacts • Residences during infectious period if unstably housed • Sex • Race • Ethnicity • Country of birth • Time in United States, if foreign born • Primary language and preferred language • Methods of translation or interpretation
Transmission Settings and Associated Time Frames	• Living situation(s) • Employment or school • Social/recreational activities • Congregate settings (e.g., jail, homeless shelter) • Substance abuse with social implications (e.g., crack cocaine)
Tuberculosis Information	• Healthcare provider for TB (e.g., public health, private, both, other) • Anatomic site of disease • Symptoms and their dates • CXR results, presence of cavitary disease • Previous treatment with TB medications with start and stop dates and adherence • Bacteriologic results (sputum smear, culture, drug susceptibility) with dates • Previous history of TB disease and treatment • Infectious period (updated as new information arrives) • HIV infection status • HIV/AIDS registry number
Contact Investigation	• Date of initial interview with index patient • Dates of follow-up interviews with index patient

Definitions of abbreviations: AIDS = acquired immunodeficiency syndrome; CXR = chest radiograph; HIV = human immunodeficiency virus; *RVCT* = *Reports of Verified Cases of Tuberculosis*; TB = tuberculosis.

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):21.

TABLE 14: DATA ABOUT EACH CONTACT[53]

Investigator and Dates	• Contact manager or investigator • Date listed • How or why contact was listed (e.g., named by index patient) • Dates of interviews • Start and end dates for exposure (updated as new information arrives)
Identifiers	• Name and aliases • For minors and dependents: guardian information • Social security number • Date of birth • Locating information and emergency contacts • Sex • Race • Ethnicity • Country of birth • Time in United States, if foreign born • Primary language and preferred language • Methods of translation or interpretation
Exposure	• Relationship/connection to index patient • Social affiliations (e.g., work, school, church, clubs, activities) • Environmental information about exposure settings (e.g., room size, ventilation) • Frequency, duration, and time frame of interactions
Medical History and Risk Factors	• Prior history of TB disease or LTBI, and documentation • BCG vaccination and date • Medical risk factors for progression of infection to TB disease† • Population risk factors for prevalent *M. tuberculosis* infection†
Evaluation for Tuberculosis Disease and Latent Tuberculosis Infection	• Healthcare provider for TB (e.g., public health, private, both, other) • Symptoms suggesting TB disease • TSTs, with dates, reagents and lot numbers, reaction measurement and/or IGRA results with dates and results • CXR results with dates • Bacteriologic results with dates • HIV infection status • Final diagnostic classifications for LTBI or TB disease

Treatment Information for Contacts with Latent Tuberculosis Infection	• Dates of treatment • Treatment regimen (medications, dosing schedule, any changes to these) • Methods of supervising treatment (DOT, etc.) • Adverse reactions (specify each) • Interruptions in regimen and dates • Outcome of treatment (completion, etc.) • If treatment not completed, reason†
Definitions of abbreviations: BCG = Bacille Calmette-Guérin; CXR = chest radiograph; DOT = directly observed therapy; HIV = human immunodeficiency virus; IGRA=Interferon Gamma Release Assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.	

Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):21.

Evaluation of a Contact Investigation

Summarize the results of a contact investigation to report by priority the total number of contacts who were identified, tested, started therapy, and completed therapy.

For more information regarding use of this evaluation framework, see the CDC Program Evaluation Workgroup's Web site at http://www.cdc.gov/eval/framework.htm.

Outbreak Investigation

If data from a contact investigation or surveillance indicate a potential outbreak, conduct an outbreak investigation. A tuberculosis (TB) outbreak warns of potential extensive transmission. An outbreak implies that (1) a TB patient was contagious, (2) contacts were exposed significantly, and (3) the interval since exposure has been sufficient for infection to progress to disease. An outbreak investigation involves several overlapping contact investigations, with a surge in the need for public health resources. More emphasis on active case finding is recommended, which sometimes means that more contacts than usual should have chest radiographs and specimen collection for mycobacteriology.

Definition of a Tuberculosis Outbreak

Definitions for a *TB outbreak* are relative to the local context. Outbreak cases can be distinguished from other cases only when certain associations in time, location, patient characteristics, or *Mycobacterium tuberculosis* attributes (e.g., drug resistance or genotype) become apparent. In low-incidence jurisdictions, any temporal cluster is suspicious for an outbreak. A working definition of a potential *TB outbreak* is helpful for planning and response, and may include any of the following six criteria (based on surveillance and epidemiology):

1. An increase in TB cases has occurred which is above the expected number of TB cases
2. During and because of a contact investigation, two or more contacts are identified as having TB disease, regardless of their assigned priority (i.e., high, medium, or low priority)
3. Any two or more cases occurring within one year of each other are discovered to be linked, and the linkage is established outside of a contact investigation (e.g., two patients who received a diagnosis of TB disease outside a contact investigation are found to work in the same office and only one or neither of the persons was listed as a contact to the other)
4. A genotype cluster leads to discovery of one or more verified transmission links that were missed during a contact investigation within the prior two years

Criteria based on program resources:

5. Transmission is continuing despite adequate control efforts by the TB control program
6. Contact investigation associated with increased cases requires additional outside help

View an example of a Health Advisory.

Deoxyribonucleic Acid Genotyping (DNA)

Deoxyribonucleic acid (DNA) genotyping is a laboratory technique used by public health agencies to distinguish between different strains of *M. tuberculosis*. Characterization of *M. tuberculosis* with DNA genotyping is a powerful tool which is useful for the following activities;

1. Surveillance of potential outbreaks
2. Confirming TB cases linked by traditional epidemiologic methods
3. Identifying clusters of patients infected with genetically related or identical strains of *M. tuberculosis* and determining common sources of infection
4. Guiding contact investigations and the appropriate use of preventive therapy
5. Identifying laboratory cross-contamination as the cause of misdiagnosis

When used to track the transmission of a specific strain, DNA genotyping can help assess the effectiveness of TB control programs, a particularly useful methodology for use in areas with low TB incidence.

The use of genotyping results can confirm linkages between cases. An outbreak increases the urgency of investigations and will put greater demands on the local health jurisdiction. Therefore, corroboration of a suspected linkage between cases by genotyping results is a valuable tool to use in the decision to intensify an investigation. An epidemiologic investigation is required for determining probable transmission linkages even if genotypes match.

Any secondary case that is unexpectedly linked to a known index patient represents a potential failure in the contact investigation; in such cases, reassess the original investigation to determine whether the strategy for finding contacts was optimal and whether the priorities were valid. If a secondary case occurred because treatment for a known contact with latent tuberculosis infection (LTBI) was not started or completed, review the strategies for treatment and completion.

For more information regarding Deoxyribonucleic Acid Genotyping, refer to National TB Controllers Association/CDC Advisory Group on Tuberculosis Genotyping. *Guide to the Application of Genotyping to Tuberculosis Prevention and Control*. Atlanta, GA: US Department of Health and Human Services, CDC; June 2004. Available at:
http://www.cdc.gov/tb/programs/genotyping/images/TBGenotypingGuide_June2004.pdf

For information on Restriction Fragment Length Polymorphism (RFLP) see:
http://www.cdc.gov/tb/programs/genotyping/Chap5/5_Developing_3c_RFLP.htm

Resources and References

Resources

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[43] CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):10.

[44] CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54 (No. RR-15):13.

[45] CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):10.

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[52] CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):21.

[53] CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):21.

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For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

Laboratory Services

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Forms Used in this Section

- QFT: TB Control Guidelines for Public Health Staff (Thurston County)
- Sputum Collection (Chelan/Douglas County)
- Tuberculosis Screening Guidelines

Introduction

Purpose

Use this section to do the following:

- Obtain contact information for laboratories
- Determine which tests are available and the turnaround times
- Identify which laboratory performs a specific test

The diagnosis of tuberculosis (TB), management of patients with the disease, and public health TB control services rely on accurate laboratory tests. Laboratory services are an essential component of effective TB control, providing key information to clinicians (for patient care) and public health agencies (for control services).[1]

Policy

Public health laboratories should ensure that clinicians and public health agencies within their jurisdictions have ready access to reliable laboratory tests for diagnosis and treatment of TB.[2]

Effective TB control requires timely, complete, and accurate communication among the laboratory system, TB control program, and healthcare provider.[3]

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see the Notifiable Conditions Guidelines at, http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

Laboratory Contact Information

To locate and contact a laboratory, refer to Table 1: Laboratory Contact Information**.** For the list of the tests performed at each laboratory, refer to Table 2: Available Laboratory Tests.

TABLE 1: LABORATORY CONTACT INFORMATION

Roles and Responsibilities	Contact Information
State Laboratory Full-service mycobacteriology laboratory. Accepts primary specimens and referral isolates from CoreLabs for identification and susceptibility testing of *Mycobacterium tuberculosis*. Statewide coordination of genotyping for positive cultures. Serves as a consultant for questions involving mycobacterium laboratory testing. Open Monday – Friday 8am – 5 pm. Closed on national holidays.	Washington State Department of Health Public Health Laboratories 1610 NE 150th St. Shoreline, WA 98155 (King County) http://www.doh.wa.gov/PublicHealthand HealthcareProviders/PublicHealthLaboratories.aspx Supervisor: 206-418-5474 TB Lab Lead: 206-418-5473
Private and Local Public Health Laboratories Laboratories on the following list provide primary specimen smear and culture testing for mycobacteria. Most refer isolates either to a CoreLab (reference Lab) or to the Washington State Department of Health Public Health Laboratories for identification and susceptibility testing.	Children's Hospital and Regional Medical Center (Hospital) 4800 Sand Point Way NE Seattle, WA 98105 (King County) Ph: 206-987-2589 Fax: 206-987-3840 Deaconess Medical Center – Spokane (Hospital) W 800 Fifth Ave Spokane, WA 99210 (Spokane County) Ph: 509-473-7410 Fax: 509-473-2700 Dynacare Northwest, Inc (Clinic) 550 17th Ave Ste 310 Seattle, WA 98122 (King County) Ph: 206-861-7235 Fax: 206-861-7367 Group Health ACC Lab (HMO) 12400 E. Marginal Way S. Tukwila, WA 98168 (King County) Ph: 206-901-4500 Fax: 206-901-4501

Roles and Responsibilities	Contact Information
Private and Local Public Health Laboratories Laboratories on the following list provide primary specimen smear and culture testing for mycobacteria. Most refer isolates either to a CoreLab (reference Lab) or to the Washington State Department of Health Public Health Laboratories for identification and susceptibility testing.	Harborview Medical Center (Hospital) 325 9th Ave Box 259743 Seattle, WA 98104 (King County) Ph: 206-731-3451 Fax: 206-731-8556 Molecular Epidemiology, Inc. 15300 Bothell Way N.E. Lake Forest Park, WA 98155 206-522-0362 Multicare Medical Center Laboratories NW (Hospital) 315 S. MLK Jr. Way Tacoma, WA 98415 (Pierce County) Ph: 253-403-1370 Fax: 253-403-1357 Oregon Medical Laboratory PO Box 77003 Eugene, Oregon 97401 Ph: 541-334-8010 or 1-800-342-2971 PAML-Pathology Associates Medical Laboratories 110 W. Cliff Ave Spokane, WA 99204 (Statewide) Ph: PAML Client Services 800-541-7891 Bellevue/Seattle Client Services 888-472-2522 Olympia Client Services 888-910-6156 Fax: 509-924-0002 Providence Everett Medical Center – Pacific (Hospital) 916 Pacific Ave. Everett, WA 98201 (Snohomish County) Ph: 425-258-7701 Fax: 425-258-7024

Roles and Responsibilities	Contact Information
Private and Local Public Health Laboratories Laboratories on the following list provide primary specimen smear and culture testing for mycobacteria. Most refer isolates either to a CoreLab (reference Lab) or to the Washington State Department of Health Public Health Laboratories for identification and susceptibility testing.	Quest Diagnostics-Seattle 1737 Airport Way S Suite 200 Seattle, WA 98134-1636 Ph: 206-623-8100 Fax: 206-224-8370 Sacred Heart Medical Center (Hospital) W 101 Eighth Ave. Spokane, WA 99204 (Spokane County) Ph: 509-474-3065 Fax: 509-474-2052 Seattle-King County Department of Public Health Laboratory (Health Department) 325 Ninth Ave, #359973 Seattle, WA 98104 (King County) Ph: 206-744-8950 Fax: 206-731-8963 Spokane Regional Health District Laboratory (Health Department) 1101 W. College Ave #210 Spokane, WA 99201 (Spokane County) Ph: 509-324-1440 Fax: 509-324-1492 St. John's Medical Center (Hospital) 1615 Delaware St. Longview, WA 98632 (Cowlitz County) Ph: 360-636-4868 Fax: 360-636-4916 St. Mary Medical Center (Hospital) 401 W. Poplar Walla Walla, WA 99362 (Walla Walla County) Ph: 509-525-3320 Fax: 509-522-5724 Stevens Hospital Laboratory (Hospital) 21601 76th Ave. W Edmonds, WA 98026 (Snohomish County) Ph: 425-640-4120 Fax: 425-640-4426

Roles and Responsibilities	Contact Information
Private and Local Public Health Laboratories Laboratories on the following list provide primary specimen smear and culture testing for mycobacteria. Most refer isolates either to a CoreLab (reference Lab) or to the Washington State Department of Health Public Health Laboratories for identification and susceptibility testing.	University of Washington Medical Center (Hospital) LAB MED BOX 357110 1959 NE Pacific St. Seattle, WA 98195 (King County) Ph: 206-616-8872 Fax: 206-616-8980 Virginia Mason Medical Center (Hospital) 1100 9th Ave – C6LAB Seattle, WA 98111 (King County) Ph: 206-223-6850 Fax: 206-223-7540 Yakima Regional Medical Center (Hospital) 110 S. 9th Ave Yakima, WA 98902 (Yakima County) Ph: 509-575-5035 Fax: 509-454-6193 Yakima Valley Memorial Hospital Laboratory (Hospital) 2811 Tieton Dr. Yakima, WA 98902 (Yakima County) Ph: 509-575-8000 Fax: 509-575-8816

Available Laboratory Tests

The laboratory tests listed below in Table 2 are available where noted.

When performing tests for the diagnosis of mycobacterial infection, acid-fast bacilli smear and culture **and** sensitivities must be ordered.

At the Washington State Department of Health Public Health Laboratory, culture identification is automatically performed on any isolate, and first-line susceptibility testing is automatically performed on all initial *Mycobacterium tuberculosis* complex isolates.

TABLE 2: AVAILABLE LABORATORY TESTS

Test	Laboratory	Turnaround Time (when available)
Interferon gamma release assay (IGRAs) for diagnosis latent TB infection (LTBI) (blood test)	Evergreen Hospital 12040 NE 128th St Kirkland, WA 98034 Ph: 425-899-3900 Fax: 425-899-3901 Overlake Hospital Medical Center 1135 116th Ave NE Ste 170 Bellevue, WA 98004 425-688-5106 PAML – Pathology Associates Medical Laboratories 110 W Cliff Ave Spokane, WA 99204 PAML Client Services (statewide): 800-541-7891 Bellevue/Seattle: 888-472-2522 Olympia: 888-910-6156 Fax: 509-924-0002 Courier Services: 800-541-7891 Providence Everett 916 Pacific Avenue Everett, WA 98201 425-261-2000 Providence St. Peter Hospital Clinical Laboratory 413 Lilly Road NE Olympia, WA 98506 360-493-5181	

Test	Laboratory	Turnaround Time (when available)
	Public Health – Seattle and King County 325 Ninth Ave Seattle, WA 98104 Ph: 206-744-8950 Fax: 206-731-8963 Quest Diagnostics 1737 Airport Way S, Suite 200 Seattle, WA 206-623-8100 Seattle Children's 4800 Sand Point Way NE Seattle, WA 98105 206-987-2000 866-987-2000 (Toll Free) Spokane Regional Health District Laboratory 1101 W. College Ave Spokane, WA 99201 509-324-1440 Tacoma General Hospital (Laboratories Northwest) 1003 South 5th – 4th Floor Tacoma, WA 98405 Tri-Cities Laboratory 7131 West Grandridge Blvd. Kennewick, WA 99336 509-736-0100 UW Medical Center 1959 NE Pacific St Seattle, WA 98195 206-598-6131	
Acid-fast bacilli (AFB) smear	Washington State Department of Health Public Health Laboratories Refer to list of private labs that provide testing for mycobacteria (Table 1)	Within 24 hours from receipt of specimen in the laboratory • Monday through Friday • See (10.14) for sending specimens

Test	Laboratory	Turnaround Time (when available)
Culture	Washington State Department of Health Public Health Laboratories Refer to list of private and local public health labs that provide testing for mycobacteria (Table 1)	Cultures are incubated for up to 8 weeks before reported as negative. Time to detection of mycobacterial growth is dependent on growth rate. Ideally, mycobacterial growth should be detected within 14 days of culture set up, although this is dependent upon many factors, including overgrowth by other organisms, etc.
Culture identification	Washington State Department of Health Public Health Laboratories: Refer to list of private and local public health labs that provide testing for mycobacteria (Table 1)	The goal for *M.tuberculosis* complex identification should be within 21 days of culture set up. Time to *M. tuberculosis* complex identification is dependent upon growth rate.
Drug susceptibility	First line drugs: Isoniazid, Rifampin, ethambutol, Streptomycin Washington State Department of Health Public Health Laboratories, Harborview Medical Center, Sacred Heart Medical Center PZA: PHL and Sacred Heart Medical Center Second line drugs: PHL	Ideally, results of first-line drugs should be available within 30 days from specimen receipt in the laboratory, but this is dependent on many factors (for example, growth rate and presence of other organisms which must be eliminated to provide a pure culture for testing). An additional 3-4 weeks is needed for the confirmation of resistance and testing for the second line anti-TB drugs.
Hepatic enzymes or up to 8 clinical, multichannel chemistry panel (that includes aspartate aminotransferase [AST], alanine aminotransferase [ALT], lactate dehydrogenase [LDH], total and direct bilirubin, alkaline phosphatase, uric acid, and calcium)	Refer to list of private labs that provide testing for mycobacteria (Table 1) or use a local lab of your choice	Check with Lab

Test	Laboratory	Turnaround Time (when available)
Uric acid	Refer to list of private labs that provide testing for mycobacteria (Table 1) or use a local lab of your choice	Check with Lab
Complete blood count (CBC) and platelets	Refer to list of private labs that provide testing for mycobacteria (Table 1) or use a local lab of your choice	Check with Lab
Kidney function	Refer to list of private labs that provide testing for mycobacteria (Table 1) or use a local lab of your choice	Check with Lab
PCR	UW, see link http://depts.washington.edu/molmicdx/mdx/available_tests.shtml	Check with Lab
Epidemiologic Monitoring		
Genotyping of positive cultures for MTB. For information on Restriction Fragment Length Polymorphism (RFLP) see: http://www.cdc.gov/tb/programs/genotyping/Chap5/5_Developing_3c_RFLP.htm	Washington State Department of Health Public Health Laboratories for referral to the Berkeley testing site (Referral is automatic)	Ideally 2 to 4 weeks from receipt of specimen at the Berkeley Laboratory Results reported to LHJ by WA State TB Services

See Notifiable conditions and the health care provider (WAC 246-101-101)

And Notifiable conditions and laboratories (WAC 246-101-201)

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

TABLE 3: LABORATORY TURN AROUND TIMES FOR PHL

Test	Type	Results Available	Results sent to clinician and LHJ
Direct tests	Positive smear	24-48 hours	Phoned and faxed within 24 hours by PHL
	Negative smear	24-48 hours	Faxed within 24 hours by PHL
Culture results	AFB Positive Cultures	1-4 weeks, ideally within 14 days of culture set up	Result phoned, all results faxed within 24 hours by PHL.
	AFB Negative Cultures	Up to 8 weeks	Faxed within 24 hours by PHL.
	Genetic Probe Test for MTB, MAC, M. gordonae and M. kansasii	Done weekly on AFB positive cultures, usually within 21 days of culture set up.	Phoned and faxed within 24 hours by PHL.
	Biochemical analysis for mycobacteria other than those listed above (considered atypical or MOTT Mycobacteria Other Than Tuberculosis)	2-3 months	Faxed by PHL.
Drug Susceptibility	Performed on confirmed MTBC cultures:		
	Bactec* (primary drugs)	7-10 days	Faxed within 24 hours by PHL.
	Plate method ** (second line drugs and confirmation of resistance to primary drugs)	Up to 4 weeks	Faxed within 24 hours by PHL.

* Bactec method: Streptomycin, Isoniazid, Rifampin, Ethambutol, Pyrazinamide
** Plate method: Streptomycin, Isoniazid, Rifampin, Ethambutol, Ethionamide, P-aminosalicylic acid, Oflaxacin and Amikacin.

Note: Reports on specimens from Harborview Medical Center will be sent to DOH TB Services. TB Services will ascertain the patients' county of residence and fax to the appropriate county LHJ.

To understand the evaluation process in diagnosing TB disease and LTBI, view the "Tuberculosis Screening Guidelines" provided on page **4.6.**

Specimen Collection

For an explanation of proper specimen collection and submission, see instructions at the Washington State Department of Health Public Health Laboratory Website: http://www.doh.wa.gov/PublicHealthandHealthcareProviders/PublicHealthLaboratories.aspx

Sputum is phlegm from deep in the lungs. The important characteristics needed in sputum specimens are freshness and actual sputum, rather than saliva. An early morning specimen is best, therefore, when collecting a set of three sputum specimens, at least one of them should be an early morning specimen.

To isolate mycobacteria from clinical materials successfully, handle specimens carefully after collection. For optimal results, collect specimens in clean, sterile containers and keep them in conditions (refrigeration) that inhibit the growth of contaminating organisms, since most specimens will contain bacteria other than mycobacteria.[4]

Washington State Department of Health Public Health Laboratories (PHL)

At Washington State Department of Health Public Health Laboratories, culture identification is automatically performed on all isolates, and first-line susceptibility testing is automatically performed on all initial *Mycobacterium tuberculosis* complex isolates.

Sputum specimen kits are available from the Washington State Department of Health Public Health Laboratories (WSPHL) by calling the PHL mailroom **206-418-5579**.

Washington State Department of Health Public Health Laboratories
Mailroom Services
1610 N.E. 150th St.
Shoreline, WA 98155

Ph: 206-418-5579
Fax: 206-418-5405

When sending the sample to WSPHL use only the unique sputum specimen kits distributed by WSPHL. Keep the kits intact until used, as all necessary items are contained in the kit. Do not use urine cups. Follow the packing instructions exactly. If the specimen leaks, it cannot be tested and the lab area must be decontaminated. If using another lab (Table 1) contact them for collection supplies.

If the patient or someone helping the patient will be shipping the specimen, assure that he/she understands all of the specific steps to follow in collecting and preparing the specimen for shipping.

Information regarding the TB Specimen Collection kits can be found at: http://www.doh.wa.gov/Portals/1/Documents/5200/SpecCollTB.pdf (TB Specimen Collection Kit)

For more information regarding sputum collection, please see Sputum Collection, located in the **FORMS** section of the manual.

Instructions for collecting and sending specimens to PHL

1. Instruct the patient to collect the sputum specimen first thing in the morning (if possible) after rinsing the mouth with water and spitting the water out into the sink.
2. Instruct the patient to cough deeply and spit the coughed up material into the specimen tube.
3. Screw the cap down tightly so the specimen tube doesn't leak.
4. Wash the outside of the specimen tube with soap and water, then dry.
5. Be sure that the specimen tube is labeled with the patient's name and the date (and the time the specimen was collected, if more than one specimen is collected on the same day).
6. Wrap absorbent material around the specimen tube.
7. Place the wrapped specimen tube in the specimen bag.
8. Seal the specimen bag with the attached "twist-tie."
9. Place cotton or other cushioning material in the bottom of the small mailing container.
10. Place the specimen tube (in its bag) into the small mailing container and screw the cap on tightly.
11. Assure that **all** information including the patient's address is provided on the PHL requisition form.
12. Wrap the completed laboratory requisition form around the outside of the small mailing container and secure with a rubber band.
13. Place the small mailing container into the large mailing container and screw the cap on tightly.
14. Ship the appropriately packaged container to the public health lab. (The address is on the container)

Med Ex now delivering packages from Greyhound Bus on Saturdays

PHL mailroom has made arrangements with Greyhound and Med Ex for an automatic 10:00am pickup on Saturdays. Med Ex should arrive at the lab between 10:00am-12:00 noon along with other courier deliveries.

Please encourage shippers to have their packages at the Seattle bus station no later than 9:30am on Saturday. This will help us ensure that their packages will be delivered to the PHL in a timely manner.

Refer to Table 4 on the following page to review the methods used to collect various specimens and the type of specimens obtained for pulmonary tuberculosis (TB).

During procedures in which aerosols may be produced, use appropriate respiratory protection and environmental controls. For more information, refer to the CDC's "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

Other useful links:

- WAC 246-101 Notifiable Conditions
  - Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx
- WAC 246-320-265 Hospital Infection Control Program
- WAC 296-800-160 Personal Protective Equipment
- WAC 296-842-100 through 300 Respirators
- WAC 388-97—140,147, 155 Infection Control Nursing Homes
- WRD 11.35 Tuberculosis Control in Health Care Settings
- WRD 11.36 Tuberculosis Control in Correctional Facilities
- DOC 670-030 Offender Tuberculosis Program
- DOC 670.000 Communicable Disease and Infection Control Program (employees)

TABLE 4: SPECIMEN COLLECTION METHODS AND TYPES FOR PULMONARY TUBERCULOSIS

Pulmonary Tuberculosis Collection Method	Specimen Type
Spontaneous sputum collection occurs when the patient can cough up sputum without extra assistance.	• 5–10 ml of sputum from deep in the lung
Induced sputum collection should be considered if a patient needs assistance in bringing up sputum.*	• 5–10 ml of sputum from deep in the lung
Gastric aspirates can be submitted for the diagnosis of pulmonary tuberculosis (TB) in persons who cannot produce sputum. (This applies primarily to young children.)	• 50 ml of gastric contents
Bronchoscopy can be used in the following situations: • If a patient cannot produce sputum by the above three methods[5] or • If a patient has a substantial risk of drug-resistant TB and has initial routine studies that are negative[6] or • In a patient in whom there is suspicion of endobroncheal TB[7] or • If a variety of clinical specimens for the diagnosis of pulmonary TB or other possible diseases need to be obtained	• Bronchial washings • Bronchoalveolar lavage • Transbronchial biopsy
* It is important to specify if the sputum is induced or not, because induced sputum is “more watery” and appears to be just saliva. Some laboratories may throw out induced sputum and report it as an inadequate specimen.	

Refer to Table 5 for collection methods and specimen types for extrapulmonary TB.

TABLE 5: SPECIMEN COLLECTION METHODS AND TYPES FOR EXTRAPULMONARY TUBERCULOSIS

Extrapulmonary Tuberculosis		
Collection Method	Specimen Type	
Extrapulmonary specimen collection from tissue and other body fluids can be submitted for the diagnosis of extrapulmonary tuberculosis.	Examples of tissues (biopsy)* • Lymph node • Pleura • Bone/joint • Kidney • Peritoneum • Pericardium	Examples of fluids • Pleural • Cerebrospinal • Blood • Urine • Synovial • Peritoneal • Pericardial
* Do not place tissue specimens in formalin.		

How to Perform Spontaneous Sputum Collection at a Healthcare Facility

Refer to the Washington State Department of Health Public Health Laboratories sub-section under “Specimen Collection” (**10.13**)

1. Collect the specimen in a specialized room or booth designed for cough-inducing procedures (negative air pressure).
2. Put a mark at the 5 ml level on the sputum tube (if not already marked) to show the patient the minimum amount of sputum needed. (Most laboratories consider 5 to 10 ml an adequate amount).
3. Instruct the patient on how to collect the sputum sample (Refer to detailed instructions under Sputum Collection – PHL).
4. Before shipping, make sure the specimen container and laboratory requisition are filled out **completely, including the patient’s address.** On the specimen container, record the patient’s name and the date and time of collection. (Time of collection is especially important when more than one sputum sample is being collected in the same day).
5. Use the State of Washington Department of Health Public Health Laboratories Mycobacteriology Laboratory Requisition form (or other laboratory-specific requisition for

other laboratories). The PHL requisition is included in the sputum collection kits which can be ordered from the PHL. An example of the requisition can be found at http://www.doh.wa.gov/Portals/1/Documents/5230/302-014-MycoTB.pdf

Information regarding the kits can be found at:
http://www.doh.wa.gov/Portals/1/Documents/5200/SpecCollTB.pdf

(TB Specimen Collection Kit)

It is especially important to **specify if the sputum is induced or not**, because an induced sputum generally is "more watery" and appears to be just saliva. Some private laboratories may throw out the specimen and report it as an "inadequate specimen."

6. Make sure the specimen and laboratory requisition are packaged into appropriate shipping containers, per laboratory instructions.

Refer to the "Specimen Collection" (**10.14**) topic and the "Specimen Shipment" (**10.25**) topic both in this section of the manual.

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at
http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at
http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

7. If possible, send the specimen on the day it is collected. If this is not possible, refrigerate the specimen until it is sent on the next day.

8. Do not save specimens to ship all three on the same day; instead, ship each one as soon as possible after collection.

9. Use the most rapid method of shipping the specimen(s) to PHL.

Make every effort to submit specimens to PHL or other laboratory within 24 hours of collection. Normal flora can overgrow any mycobacteria in the specimen and make it unusable. Most laboratories will not run a specimen over five days old. Know how long it takes the specimen to arrive at PHL or other laboratory from the time it leaves your facility, and submit specimens accordingly.

During procedures in which aerosols may be produced, use appropriate respiratory protection and environmental controls. For more information, refer to the CDC's "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]) at: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

- WAC 246-320-265 Hospital Infection Control Program
- WAC 296-800-160 Personal Protective Equipment
- WAC 296-842-100 through 300 Respirators
- WAC 388-97—140,147, 155 Infection Control Nursing Homes
- WRD 11.35 Tuberculosis Control in Health Care Settings
- WRD 11.36 Tuberculosis Control in Correctional Facilities
- DOC 670-030 Offender Tuberculosis Program
- DOC 670.000 Communicable Disease and Infection Control Program (employees)

How to Direct a Patient to Perform Spontaneous Sputum Collection at Home

If a patient will be collecting sputum specimens at home, provide the following guidance:

1. Put a mark at the 5 ml level on the sputum tubes (if not already marked) to show the patient the minimum amount of sputum needed. (Most laboratories consider 5 to 10 ml an adequate amount).

2. Review with the patient how to collect the sputum sample. (Refer to detailed instructions under Sputum Collection – Washington State Department of Health Public Health Laboratories).

3. Make arrangements for a healthcare worker to pick up the specimen or for the patient, a family member, or a friend to drop off the specimen. If the patient or someone helping the patient will be shipping the specimen, assure that he/she understands all of the specific steps to follow in collecting and preparing the specimen for shipping.

Refer to the Washington State Department of Health Public Health Laboratories sub-section under "Specimen Collection" (**10.13**)

Induced Sputum Collection at a Healthcare Facility

If the patient cannot produce sputum spontaneously, make arrangements for an induced sputum to be collected at a facility. Facilities where sputum can be collected include the respiratory therapy department of a local hospital, TB Clinic, or laboratory. Collect the specimen in a specialized room or booth (negative air pressure) designed for cough-inducing procedures.

Facilities should have appropriate respiratory protection, environmental controls, and policies and procedures in place to prevent transmission of TB to other persons. For further information regarding infection control during sputum collection, refer to the Infection Control Section: environmental controls, respiratory protection and facility requirements for infection control policies and procedures.

During procedures in which aerosols may be produced, use appropriate respiratory protection and environmental controls. For more information, refer to the CDC's "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]) at:

http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

- WAC 246-320-265 Hospital Infection Control Program
- WAC 296-800-160 Personal Protective Equipment
- WAC 296-842-100 through 300 Respirators

Use the State of Washington Department of Health Public Health Laboratories Mycobacteriology Laboratory Requisition form (or other laboratory-specific requisition for other laboratories.) The PHL requisition is included in the sputum collection kits which can be ordered from the PHL. An example of the requisition can be found at :
http://www.doh.wa.gov/Portals/1/Documents/5230/302-014-MycoTB.pdf

Information regarding the PHL sputum collection kits be found at:
http://www.doh.wa.gov/Portals/1/Documents/5200/SpecCollTB.pdf

(TB Specimen Collection Kit)

How to Collect Gastric Aspirates

Gastric aspirates are most commonly collected on children, however this procedure may also be used in adults.

The following are basic guidelines for collecting gastric aspirates:

Patient Preparation:

4. The patient is to have nothing by mouth after midnight.
5. The family (patient) should come to the clinic first thing in the morning.
6. Place a nasal gastric tube in the patient. Do not use surgilube as it is bacteriostatic. Use as large a bore NG tube as is comfortable (minimum 10 french). Avoid too deep a placement to prevent passage through the pylorus.

Sample Collection:

7. Aspirate the stomach contents. If less than 10 cc of mucus is aspirated, instill 20-30 cc of sterile water into the tube and quickly withdraw. (Note: the organism is most viable when not exposed to saline or preservatives; the kind of sterile water used for infant feeding is fine). Reposition the tube and/or the patient to maximize the yield of gastric contents.
8. Place the gastric aspirates in a special bicarbonate-containing gastric aspirate tube or regular specimen cup.
9. Transport the specimen to the microbiology lab. If a special bicarbonate-containing tube or cup is not available, the lab must neutralize the stomach acid with bicarbonate within ½ hour.

For additional information on how to collect a gastric aspirate and prepare the specimen for transport, see the guide and Curry International Tuberculosis Center's online video *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure* at:

http://www.currytbcenter.ucsf.edu/catalogue/epub/index.cfm?tableName=GAP

Bronchoscopy or Collection of Extrapulmonary Specimens

If TB staff are consulting with physicians before the specimens are collected, the physician should be reminded to send part of the specimen (not in formalin) to the microbiology laboratory for acid-fast bacilli (AFB) smear and culture, in addition to any other tests or pathology examinations the physician plans to obtain. In addition, a post-bronchoscopy sputum specimen should be sent for AFB smear and culture. Bronchoscopy and extrapulmonary specimens will be collected by the physician and facility performing the procedure.

The Curry International Tuberculosis Center has developed a web presentation on "Practical Solutions for TB Infection Control: Infectiousness and Isolation" available at http://www.currytbcenter.ucsf.edu/tbicweb/

Interferon Gamma Release Assay (IGRA) QuantiFERON®- TB-Gold In-Tube Testing (QFT-G) the T-SPOT®.*TB* Test

The QuantiFERON®-TB Gold In-Tube Test (QFT-G) is an interferon gamma release assay (IGRA) which tests blood for the presence of *M. tuberculosis* infection. The T-SPOT®.*TB* test is an IGRA that enumerates the response of effector T cells that have been sensitized to Mycobacterium tuberculosis. For patients with a previous positive TST reaction, an IGRA can be done if there is suspicion that the TST result was a false positive. In addition, the IGRA test is not affected by past bacille of Calmette-Guerin (BCG) vaccination and may eliminate the unnecessary treatment of patients with BCG-related-false-positive results on a TST.

The advantages of the IGRA, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory using standardized analysis methods, the variability in results associated with skin test reading can be eliminated.

However, the IGRA test has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory within 16 hours.

CDC recommends that the IGRA may be used in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants, and sequential-testing surveillance programs for infection control (e.g., those for health-care workers). The use of IGRA in pediatric populations is still being researched, but looks promising. The CDC guidelines can be found at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.htm

Guidelines for the use of the IGRA test developed by Thurston County are available in the forms section of this manual. http://www.doh.wa.gov/cfh/TB/Manual/Forms/TBControlGuidelines.pdf

For a list of laboratories offering the IGRA test in Washington State, see Table 2.

CDC released new Interferon Gamma Release Assays (IGRA) guidelines on June 25, 2010, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" *(MMWR* 2010; 59 [No. RR-5];1-25) at http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf. CDC has also developed the Interferon-Gamma Release Assays (fact sheet) that will assist you in learning more about IGRAs. http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm

A single IGRA test is used in place of (and not in addition to) the TST in screening of healthcare workers.

For more information regarding QFT healthcare worker guidelines see QFT: TB Control Guidelines for Public Health Staff (Forms Section)

Find answers to common questions posed by healthcare professionals on the use of QFT at http://www.cellestis.com/IRM/Company/ShowPage.aspx?CPID=1588&EID=60701344.

For more information on the T-SPOT®.*TB* test, visit http://www.oxfordimmunotec.com/Products_North_America

Specimen Shipment

There are three main categories of transportation methods: medical couriers, ground transportation, and air transportation. Shipment of specimens is further categorized by their likelihood of causing infection if improperly handled. Each category requires different packaging requirements to provide increased levels of protection against leaks and contamination.

The following is for informational purposes:

Category A

Category A specimen handling applies only to laboratories because they deal with pure mycobacterial cultures which are classified as "dangerous goods." Local Health Jurisdictions and other healthcare providers will not be handling these specimens.

Category A: Pure mycobacterial cultures (or culture isolates suspected of being mycobacteria) are classified as Category A Infectious Substances and can be transported only by a medical courier or shipped by private carrier as dangerous goods. Category A Infectious Substances cannot be mailed through the US Postal Service.

Shipment of dangerous goods by USPS is regulated by the US Department of Transportation. Specific shipping instructions from the Centers for Disease Control and Prevention (CDC) can be found in the publication: US Department of Health and Human Services (DHHS) *Public Health Mycobacteriology: A Guide for the Level III Laboratory*. Packaging and shipment of specimens by USPS should meet the following regulations:

- Public Health Service/CDC: 42 CFR, Part 72—Interstate Shipment of Etiologic Agents at http://www.cdc.gov/od/ohs/biosfty/shipregs.htm
- USPS: 39 CFR and USPS Domestic Mail Manual C023.1.1, International Mail Manual 135, and USPS Publication 52
- US Department of Transportation: 49 CFR, Parts 171–185 (August 14, 2002) at http://www.access.gpo.gov/nara/cfr/waisidx_04/49cfrv2_04.html
- The Department of Labor, Occupational Safety and Health Administration (OSHA): 29 CFR 1910.1030[8]

For shipments by private carriers, follow International Air Transportation Association (IATA) instructions. *Mycobacterium tuberculosis* pure cultures are defined as infectious substances/etiologic agents when shipped by private carrier and must be shipped in packaging approved by the United Nations (UN), according to IATA Packing Instruction 602. Diagnostic specimens are defined as human or animal specimens, including excreta, secreta, blood and its components, tissue, tissue fluids, and cultures of nontuberculous mycobacteria being transported for diagnostic or investigational purposes. Diagnostic specimens must be packaged according to IATA Packing Instruction 650.[9]

Category B specimens are "raw" specimens which are handled by Local Health Jurisdictions and other healthcare providers.

Category B

Category B: Infectious Substances (raw diagnostic specimens, such as sputum, blood, or tissue) can be mailed through the US Postal Service (USPS), shipped by private carrier (e.g., Federal Express, Airborne Express, etc.), or transported by a medical courier, taxi or private vehicle.

For information regarding requirements for shipping, refer to the Washington State Department of Health Public Health Laboratories website at:
http://www.doh.wa.gov/Portals/1/Documents/5200/SpecCollTB.pdf

Shipping Training Requirements

Employers are responsible for assuring proper training for all employees with job responsibilities which include the packaging and shipping of diagnostic (clinical) specimens. This training may be conducted either at the job location or by sending employees to a course presented by the Washington State Department of Health Public Health Lab or other source for training. Documentation of training from a former employer is also acceptable. Only the employer can certify that the training is appropriate for each individual given their job responsibilities.

Training and certification should occur within 90 days of hire or assignment to a job where such knowledge is needed. Retraining should occur whenever regulatory changes indicate, or at least once every three years. Training should also be followed by demonstration of competency, either during the training course, or by the employer at the facility, which documents the validity of the training and the mastery of the content by the employee. Documentation of this training and the resulting certification must be kept throughout the entire time the individual is employed in the facility.

As part of the training process, the employer has several responsibilities:

- Training must be specific to the job duties performed by an individual.
- Retraining must be provided as needed, according to changing regulations.
- The employer must be in contact with the carrier to assure that most recent rules are met.
- The employer must keep records of the curriculum and content of each training session.
- The employer must certify that the individual has been properly trained in accordance with work responsibilities and has passed a test to assure competency.
- The employer must maintain the documentation throughout the entire course of employment of an individual.

For further information refer to:

- Washington State Department of Labor and Industries Enforcement Directive: OSHA CPL 2-2.69
- Requirements for Specimen containment: WAC 296-823-14045
- Requirements for labeling: WAC 296-823-14025
- For shipping training courses, contact the Washington State Department of Health Public Health Laboratories website at: http://www.doh.wa.lcl/AboutUs/ProgramsandServices/DiseaseControlandHealthStatistics/PublicHealthLaboratories/ContactUs.aspx
- For shipping regulations, refer to "Resources and References" at the end of this section.

For more information regarding shipping requirements, contact the following staff at the Washington State Department of Health Public Health Laboratories:

- Training Program Advisor (PHL) ph: 206-418-5404 Fax: 206-418-5445
- Training Program Manager (PHL) ph: 206-418-5401 Fax: 206-418-5445
- Training Program (PHL) ph: 206-418-5402 Fax: 206-418-5445

To obtain specimen collection and transport supplies, see the topic on "Specimen Collection" and "Specimen Shipment" in this section of the manual.

Sputum specimen kits are available from the Washington State Department of Health Public Health Laboratories (PHL) by calling the PHL mailroom at **206-418-5579.**

Washington State Department of Health
Public Health Laboratories
Mailroom Services
1610 N.E. 150th St.
Shoreline, WA 98155

Ph: 206-418-5579
Fax: 206-418-5405

Resources and References

Resources for Laboratory Services

Detailed descriptions of recommended laboratory tests; recommendations for their correct use; and methods for collecting, handling, and transporting specimens have been published.

For more information on laboratory testing for tuberculosis (TB), see the following:

- ATS, CDC, IDSA. "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America" (*MMWR* 2005;54[No. RR-12]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5412.pdf .
- ATS, CDC, IDSA. "Diagnostic Standards and Classification of Tuberculosis in Adults and Children" (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: http://ajrccm.atsjournals.org/cgi/reprint/161/4/1376 .
- National Committee for Clinical Laboratory Standards. *Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard* [Document no. M24-A] (Wayne, PA; 2003).

Resources for Specimen Collection and Shipment

- CDC. "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf .
- CDC. *Public Health Mycobacteriology: A Guide for the Level III Laboratory* (Atlanta, GA; 1985).
- Curry International Tuberculosis Center. *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure* (Curry International Tuberculosis Center Web site). Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=ONL-06
- International Air Transport Association (IATA). IATA Web site. Available at: http://www.iata.org/index.htm .
- National Jewish Medical and Research Center. *How to Mail Specimens and Cultures to the National Jewish Mycobacteriology Laboratory* (Denver, CO: March 2005).
- National Jewish Medical and Research Center. *Instructions (for Patients) for Collecting and Mailing Sputum Specimens* (Denver, CO: March 2005).
- US Department of Transportation. Hazardous Materials: Revision to standards for infectious substances. Part III 49 CFR Part 171. Federal Register (August 14, 2002).
- USPS. *Mailing Standards of the United States Postal Service: Domestic Mail Manual* (USPS Web site). *Available* at: http://pe.usps.com/ .

In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at http://apps.leg.wa.gov/wac/default.aspx?cite=246-101

Also, see Notifiable Conditions Guidelines, at http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx

References

[1] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):18.

[2] ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19.

[3] Association of Public Health Laboratories. *The Future of TB Laboratory Services: A framework for integration/collaboration/leadership* [Association of Public Health Laboratories Web site]. 2004. Available at: http://www.aphl.org/Documents/Global_docs/tb_task_force_future.pdf

[4] ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med*. 2000;161:1376–1395.

[5] Iseman, MD. *A Clinician's Guide to Tuberculosis, 2000*. 1st ed. Philadelphia, PA: Williams & Wilkins; 2000:135–136.

[6] Iseman, MD. *A Clinician's Guide to Tuberculosis, 2000*. 1st ed. Philadelphia, PA: Williams & Wilkins; 2000:135–136.

[7] Iseman, MD. *A Clinician's Guide to Tuberculosis, 2000*. 1st ed. Philadelphia, PA: Williams & Wilkins; 2000:135–136.

[8] National Jewish Medical and Research Center. *How to Mail Specimens and Cultures to the National Jewish Mycobacteriology Laboratory.* Denver, CO; March 2005:2.

[9] National Jewish Medical and Research Center. *How to Mail Specimens and Cultures to the National Jewish Mycobacteriology Laboratory.* Denver, CO; March 2005:5–7.

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For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

Treatment of Latent Tuberculosis Infection

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Forms Used in this Section

- Chart Audit Tool
- Clinic Record (Virginia)
- Consent and Treatment Plan (Georgia)
- DOT Log (Virginia)
- Drug Interview Sheet (SHD)
- Drug-O-Gram (TPCHD)
- LTBI and Disease (Kansas)
- Medication Administration Record (MAR)
- Medication Information (Georgia)
- Medication Log
- QFT: TB Control Guidelines for Public Health Staff (Thurston County)
- Protocol and Standing Orders (SHD)
- Symptom Screen (Georgia)
- Tuberculosis Screening Guidelines

Quick Start Check List: Treatment of Latent Tuberculosis Infection

This check list is designed to assist public health nurses in treating a patient for latent tuberculosis infection. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:
Washington State TB Services
Mailing address: P.O. Box 47837 Olympia, WA 98504
Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
Diagnose latent tuberculosis infections (LTBI), ruling out tuberculosis (TB) disease	Instructions: • Diagnosis of Latent Tuberculosis Infection (6.3) • Protocol and Standing Orders (SHD) • Symptom Screen (Georgia) • LTBI and Disease (Kansas) • Chart Audit Tool
Select and appropriate treatment regimen: ☐ Assure that an appropriate treatment regimen, dosages, and duration are selected ☐ Assure that these special situations are considered: • Human immunodeficiency virus (HIV) infection • Alcoholism • Pregnancy and breastfeeding	Instructions: • Regimens (7.11 Table 1) • Dosages (7.12 Table 2) • Consent and Treatment Plan (Georgia)
Monitor the patient regularly: ☐ Assure that the patient is assessed at least monthly for • Clinical follow-up • Adherence to LTBI treatment • Adverse reactions to LTBI treatment	Instructions: • Reporting Reactions (7.15 Table 3) • Monitoring and Interactions (7.17 Table 4) The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Persons Being Treated for Latent Tuberculosis Infection," available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm Forms • Drug Interview Sheet (SHD) • Clinic Record (Virginia) • Medication Information (Georgia) • Medication Administration Record • Medication Log
Confirm the completion of treatment: ☐ Verify completion of treatment 6 to 9 months after treatment was started depending upon • Regimen • Adherence	Instructions: • Recommended Regimens (7.21 Table 5)

To understand the evaluation process in diagnosing TB disease and LTBI, view the "Tuberculosis Screening Guidelines" provided on page 4.6.

Introduction

Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Determine whom to treat for latent tuberculosis infection (LTBI)
- Select appropriate treatment regimens and dosages
- Monitor patients for adverse reactions
- Monitor patients' adherence to treatment
- Determine whether and when therapy is completed
- Provide treatment in special situations, such as when a patient is pregnant or has tuberculosis (TB)–human immunodeficiency virus (HIV) coinfection

Prevention of TB has major public health implications, so it is essential to identify and treat all those with risk factors for TB disease.[1] LTBI is the presence of *Mycobacterium tuberculosis* organisms (tubercle bacilli), with no symptoms and no radiographic or bacteriologic evidence of TB disease.[2] A person with LTBI is noninfectious but can develop active TB disease. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions associated with an increased risk for the progression of LTBI to TB disease.

To control and prevent TB, our healthcare resources and efforts in Washington State should be directed to meet the priorities outlined in the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America." One of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification and treatment of persons with LTBI at risk for progression to TB.[3]

Targeted tuberculin testing for LTBI is a strategic component of TB control that identifies persons at high risk for developing TB who would benefit by treatment of LTBI, if detected. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions that are associated with an increased risk for progress of LTBI to active TB.

Healthcare providers must communicate the risks and benefits of treatment to their patients and encourage adherence and treatment completion. Treatment of LTBI is an essential element in controlling and eliminating TB in the United States. LTBI treatment substantially reduces the risk that TB infection will progress to disease.[4] Depending upon adherence and length of treatment, completing treatment for LTBI can reduce the risk of TB disease by 65–90%.[5]

Whom to Treat

Determine whom to treat for latent tuberculosis infection (LTBI). Certain groups are at high risk of developing tuberculosis (TB) disease once infected, so make every effort to begin appropriate treatment and to ensure that these persons complete the entire course of treatment for LTBI.[6]

For a list of high-risk groups by tuberculin skin test (TST) results, see the Tuberculin Skin Test Results listings, which follow in this topic. For more information on targeted testing, see "Targeted Testing for Latent Tuberculosis Infection" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see the "Time Frames for Contact Investigation" topic in the Contact Investigation section of the manual (**9.16**) and "Guidelines for Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Several treatment regimens are available for the treatment of LTBI, and providers should discuss treatment options with their patients.[7]

For more information on treatment of LTBI, see the "Treatment Regimens and Dosages" topic in this section of the manual (**7.9**) and Treatment of Latent Tuberculosis Infection (LTBI) at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

LTBI Card: Patient's TB Testing and Treatment Record, available at http://www.umdnj.edu/globaltb/products/ltbicard.htm.

Susceptible and Vulnerable Contacts

A contact is someone who has been exposed to *M. tuberculosis* infection by sharing air space with a person with infectious TB.[8] Susceptible contacts are those who are more likely to become ill with TB disease if they are infected, and vulnerable contacts are those who could suffer severe morbidity if they progress to TB disease.[9] (These include children under 5 years of age, and those who are HIV-infected, immunocompromised or have other underlying disease processes.) Persons who are susceptible and/or vulnerable to TB disease are candidates for window period treatment, which is administering treatment for presumptive TB infection during the interval between infection and detectable skin test or positive IGRA testing. The National Tuberculosis Controllers Association (NTCA) and the CDC recommend that the window period be estimated at 8 to 10 weeks.[10] The following contacts with initially negative TST or IGRA test results should receive treatment for LTBI after TB disease has been ruled out by clinical examination and chest radiograph:

1. Contacts younger than 5 years of age (with highest priority given to those under 3 years)
2. Contacts with human immunodeficiency virus (HIV) infection or who are otherwise immunocompromised

If the second skin test or IGRA result is negative and the contact is immunocompetent (including immunocompetent young children) and no longer exposed to infectious TB, treatment for LTBI may be discontinued, and further follow-up is unnecessary. If the second test is negative but the contact is immunocompromised (e.g., with human immunodeficiency virus [HIV] infection), a course of therapy for LTBI should be completed. If the second test result is negative but the person remains in close contact with an infectious patient, treatment for LTBI should be continued if the contact is:

1. Less than 5 years old.
2. Aged 5–15 years, at the clinician's discretion.
3. HIV-seropositive or otherwise immunocompromised.[11]

Persons known to be (or suspected of being) immunocompromised, such as HIV-infected persons, should be given treatment for LTBI regardless of the TST or IGRA reaction.[12]

For more information regarding the IGRA, QuantiFERON®--TB Gold, see CDC, NTCA. "Guidelines for the investigation of contacts of persons with infectious tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf, and "Guidelines for using the QuantiFERON®- -TB Gold test for detecting Mycobacterium tuberculosis infection, United States", MMWR 2005;54(no. RR-15) at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf.

Also, see more information on this topic in QFT: TB Control Guidelines for Public Health Staff (FORMS), and "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf.

Tuberculin Skin Test Results of 5 mm or More

Persons in the following high-risk groups are candidates for treatment of LTBI if their skin test result is 5 mm or more:

- Persons with HIV infection
- Recent contacts of persons with newly diagnosed infectious TB
- Persons with fibrotic changes on their chest radiograph that are consistent with old TB
- Persons with organ transplants and other immunosuppressed patients (receiving the equivalent of 15 mg or more/day of prednisone for at least one month)[13]

Tuberculin Skin Test Results of 10 mm or More

Persons in the following high-risk groups are candidates for treatment of LTBI if their skin test result is greater than or equal to 10 mm:

- Foreign-born persons who have recently arrived (within five years) from countries with a high TB incidence or prevalence, or persons who have recently traveled to these countries (most countries in Africa, Asia, Latin America, Eastern Europe, and Russia (formerly the USSR)
- Persons who are alcoholics, who inject drugs, or who use other high-risk substances, such as crack cocaine
- Residents and employees of high-risk congregate settings, such as correctional institutions, homeless shelters, long-term residential care facilities (e.g., nursing homes, mental institutions), hospitals, and other healthcare facilities
- Mycobacteriology laboratory personnel
- Persons with medical conditions or undergoing treatments that increase the risk of TB disease (diabetes mellitus, silicosis, recent infection with *M. tuberculosis* within the past two years, bone marrow and organ transplant recipients, prolonged high-dose corticosteroid therapy and other immunosuppressive therapy, chronic renal failure, hemodialysis, some hematological disorders [e.g., leukemias and Hodgkin's disease], other specific malignancies [e.g., carcinoma of the head, neck, or lung], chronic malabsorption syndromes, weight of 10% or more below ideal body weight, and intestinal bypass or gastrectomy)
- Children less than 5 years of age
- Infants, children, and adolescents exposed to adults at high risk for developing TB disease
- Locally identified groups at high risk[14]

Tuberculin Skin Test Results of 15 mm or More[15]

Persons in the following groups may be considered for treatment of LTBI if their skin test result is greater than or equal to 15 mm. These groups should be given a lower priority for prevention efforts than the groups already listed above.

- Persons with no known risk factors for TB disease
- Healthcare workers* who are otherwise at low risk for TB disease and who received baseline testing at the beginning of employment as part of a TB screening program[16]

Treatment Regimens and Dosages

Select appropriate treatment durations, regimens, and dosages. Treatment of latent tuberculosis infection (LTBI) is an essential part of the strategy to eliminate tuberculosis (TB) in the United States. Persons with LTBI who are considered at increased risk for TB should be offered treatment.[17]

There are several treatment regimens available for the treatment of LTBI, and providers should discuss options with patients. Persons who are at especially high risk for TB, and either are suspected of nonadherence or are on an intermittent dosing regimen, should be treated using directly observed therapy (DOT). This method of treatment is especially appropriate when a household member is on DOT for TB disease or in institutions and facilities where a staff member can observe treatment.

For a list of high-risk groups, see “Targeted Testing for Latent Tuberculosis Infection” at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see “Treatment of Latent Tuberculosis Infection (LTBI)” at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf

The most current TB treatment guidelines state that frequent monitoring of a patient's treatment regimen and response to treatment is critical and can be accomplished through use of a drug-o-gram. This electronic resource provides an interface for entering patient data to create a drug-o-gram. It includes a user's guide with instructions and teaching points. http://www.umdnj.edu/ntbcweb/products/drugogram.htm

To view a sample drug-o-gram form from TPCHD, please see “Drug-O-Gram” located in the **FORMS** section of the manual.

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued "An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy." Consult these recommendations at on pages 943-947 for guidance in the following areas for the safe treatment of LTBI and TB Disease:

- **Program Infrastructure**
  Adopt these standardized approaches to develop safe treatment of LTBI and TB disease.
- **Provider Education and Resources**
  Develop these written resources, educational programs, and referral mechanisms to assure that healthcare providers have the skills, knowledge, and resources to safely diagnose and treat patients with TB disease and LTBI.
- **Pretreatment Clinical Evaluation**
  Refer here for a list of what to include in the pretreatment clinical evaluation and the initial physical examination and when to screen for viral hepatitis.
- **Patient Education**
  Follow these suggestions to improve patients' awareness of and communication about their symptoms of liver disorders. Communicate with patients in their preferred language[18] and carefully confirm that they understand the educational points being made.
- **Medication Administration and Pharmacy**
  Use these tips to distribute antituberculosis medications in ways that encourage and reinforce prompt reporting by patients of adverse effects.
- **Treatment of LTBI and Treatment of TB Disease**
  Use these recommendations to guide treatment decisions and monitoring activities. Numbered lists of recommendations provide detailed information. Three flowcharts show key data and decisions in the following areas: LTBI pretreatment clinical evaluation and counseling, monitoring for hepatotoxicity during LTBI treatment, and monitoring for hepatotoxicity during treatment of TB disease.19

Regimens

Identify an appropriate regimen for the patient using the national guidelines provided in Table 1 below.

TABLE 1: RECOMMENDED DRUG REGIMENS FOR TREATMENT OF LATENT TUBERCULOSIS INFECTION IN ADULTS[20]

Drug	Interval and Duration	Comments	Rating* (evidence)†	
			HIV–	HIV+
INH	Daily for 9 months‡ §	In HIV-infected patients, INH may be administered concurrently with nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors, or non-nucleoside reverse transcriptase inhibitors (NNRTIs).	A (II)	A (II)
	Twice weekly for 9 months‡ §	DOT must be used with twice-weekly dosing.	B (II)	B (II)
INH	Daily for 6 months§	This duration of therapy is not indicated for HIV-infected persons, those with fibrotic lesions on chest radiographs, or children.	B (I)	C (I)
	Twice weekly for 6 months§	DOT must be used with twice-weekly dosing.	B (II)	C (I)
RIF	Daily for 4 months in adults Daily for 6 months in children	RIF is used for persons who are contacts of patients with INH-resistant, RIF-susceptible TB. Some antiretroviral drugs, such as the protease inhibitors and NNRTIs, have interactions with the rifamycins. Clinicians should consult Web-based updates or experts for the latest specific recommendations. The optimal length of RIF therapy in children with LTBI is not known; however, the American Academy of Pediatrics recommends 6 months of treatment.[21]	B (II)	B (III)

Definitions of abbreviations: DOT = directly observed therapy; HIV = human immunodeficiency virus; INH = isoniazid; LTBI = latent tuberculosis infection; RIF = rifampin.

* Strength of recommendation: A = Preferred, B = Acceptable alternative, C = Offer when A and B cannot be given.

† Quality of evidence: I = Randomized clinical trial data, II = Data from clinical trials that are not randomized or were conducted in other populations, III = Expert opinion.

‡ Recommended regimen for children <18 years of age.

§ Recommended regimen for pregnant women.

Source: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):31.

The regimen of rifampin (RIF) and pyrazinamide (PZA) for two months is no longer recommended for treatment of LTBI because of its association with severe liver injury. For more information, see the CDC's "Update: Adverse Event Data and Revised American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection" (*MMWR* 2003;52[No. 31]:735) at http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf

Dosages

Once the appropriate regimen has been identified, refer to Table 2 for instructions on dosages for each drug. The information in Table 2 is taken from ATS, CDC, and Infectious Diseases Society of America (IDSA) guidelines.

TABLE 2: RECOMMENDED DOSAGES[22,23]

Drug	Preparation	Adults/ Children	Daily	Twice a Week
INH	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml)	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)
		Children (max.)	10–15 mg/kg (300 mg)	20–30 mg/kg (900 mg)
RIF	Capsule (150 mg, 300 mg); powder may be suspended for oral administration	Adults (max.)	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (max.)	10–20 mg/kg (600 mg)	10–20 mg/kg (600 mg)
Definitions of abbreviations; INH = isoniazid; RIF = rifampin.				

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):4; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):28–29.

The use of INH elixir is discouraged, as it commonly causes diarrhea and cramping in children. If children have difficulty taking medications, open capsules and crush tablets, and then hide the drugs in soft foods or liquids. Possible foods include maple syrup, hot fudge, Nutella, apple sauce, jams and jellies, spinach baby food, and chocolate whipped cream, etc. Layer the food and drug on a spoon, and teach the child to take the contents of the spoon without chewing.[24]

For consultation regarding the treatment of LTBI in persons who have been in contact with a case who is resistant to drugs in the recommended regimens, you may contact the WA State TB Services Medical Consultant 206-718-2664.

Side Effects and Adverse Reactions

The patient should be monitored by a registered nurse and/or clinician or case manager at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be consulted and the patient monitored more frequently. Blood chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done periodically. See Table 4: Monitoring and Interventions for Side Effects and Adverse Reactions in this section.

As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.[25]

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that the drugs with the highest evidence rating not be stopped without adequate justification.[26] However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy; whereas with more severe effects, the offending drug or drugs must be discontinued.[27] In addition, proper management of more serious adverse reactions often requires expert consultation.[28] A comprehensive statement on Hepatoxicity of Antituberculosis Therapy has been published by the American Thoracic Society, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

Basic Monitoring Steps

1. All healthcare workers providing treatment for latent tuberculosis infection (LTBI) should be familiar with the American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines.
   - **a.** All jurisdictions should follow the national monitoring guidelines identified in the current treatment guidelines for treatment of LTBI, “Targeting Tuberculin Testing and Treatment of Latent Tuberculosis Infection,” pages 26–29 at http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf .
   - **b.** It is also important to check for guideline updates posted on the CDC’s Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/default.htm and the list of guidelines by date at http://www.cdc.gov/tb/publications/guidelines/default.htm.
2. While on treatment, all patients should be evaluated in person, at baseline (before starting treatment), and then at least monthly for side effects and adverse reactions. For sample monitoring forms, please see the Snohomish Drug Interview Sheet, Clinic Record (Virginia), and DOT Log (Virginia) in the **Forms** section of this manual.

3. The common side effects of and adverse reactions to drugs used to treat for LTBI are listed in Table 3: Reporting Reactions to Antituberculosis Medications. Educate patients to stop the medicine and promptly report any of the symptoms or signs listed in Table 3 or any unexplained illness to the prescribing clinic immediately.
   a. If a patient reports a potentially serious adverse reaction, call the patient's provider immediately and take action according to the provider's instructions.
   b. If a patient reports a potentially less severe side effect, call the patient's provider immediately and monitor the patient.
4. If you suspect that an antituberculosis drug may be causing a particular side effect or adverse reaction:
   a. Refer to Table 4: Monitoring and Interventions for Side Effects and Adverse Reactions below.
   b. Consult with the patient's medical provider, Local Health Officer or WA State TB Services Medical Consultant (206) 718-2664.
5. If you suspect that an antituberculosis drug may be interacting with other medications that the patient is taking, refer to pages 45–47 in the "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf.
6. Document the following patient information:
   a. Review of symptoms, side effects, and adverse reactions (and any labs that were drawn)
   b. Education given
   c. Refill provided
   d. Description of any problems encountered and action taken for that visit
   e. Next appointment

For more information on Assessing and Managing the Risk of Liver Disease in the Treatment of LBTI, please see the algorithm at: http://www.heartlandntbc.org/products/assessing_and_managing_the_risk_of_liver_disease_in_the_treatment_of_ltbi.pdf

Reporting Reactions

The table below is intended for use by a healthcare worker who performs case management services. The healthcare worker should instruct the patient to report to the provider the side effects and adverse reactions listed in Table 3.

If a patient reports to a healthcare worker a potentially serious adverse reaction, the healthcare worker should call the patient's provider immediately and take action according to the provider's instructions.

If a patient reports to a healthcare worker a potentially less severe side effect, the healthcare worker should call the patient's provider immediately and monitor the patient.

TABLE 3: REPORTING REACTIONS TO ANTITUBERCULOSIS MEDICATIONS[29]

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient's provider. These signs and symptoms suggest side effects, including hepatotoxicity: • Jaundice • Dark urine • Vomiting • Abdominal pain • Fever • Visual changes • Marked clinical rash In consultation with the provider, instruct the patient to stop TB medications until evaluated by the provider.	Report the following signs and symptoms to the patient's provider **within 24 hours**: • Anorexia • Nausea • Malaise • Peripheral neuropathy: tingling or burning sensation in hands or feet • Rashes
* These lists are not all-inclusive. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf and An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf,	

NOTE: The two-month regimen of rifampin and pyrazinamide is no longer recommended due to serious and fatal hepatitis associated with this regimen.[30]

At present, the Division of Tuberculosis Elimination (DTBE) urges health departments, hospices, hospitals, jails, prisons, and private medical offices to report all severe adverse events (e.g., liver injury, pancreatitis, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for LTBI that occurred after January 1, 2004, to DTBE by calling 404-639-8401. Also, if not done previously, please call the Washington State Tuberculosis Services at 360-236-3443 to report these severe adverse events.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 4**:** Monitoring and Interventions for Side Effects and Adverse Reactions to do the following:

- Identify the side effects and adverse reactions associated with particular antituberculosis drugs
- Determine how to monitor for side effects and adverse reactions

TABLE 4: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS[31,32,33]

Antituberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Isoniazid (INH)	• Rash • Hepatic enzyme elevation • Hepatitis • Peripheral neuropathy • Mild central nervous system effects	Clinical monitoring monthly Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions • Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin), and adjust the dose if necessary. More information is available in the Official ATS Statement: Hepatotoxicity of Antibuerculosis Therapy, available at http://ajrccm.atsjournals.org/cgi/reprint/174/8/935.pdf.

Antituberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (RIF)	• Rash • Gastrointestinal upset • Hepatitis • Fever • Bleeding problems • Thrombocytopenia • Renal failure • Flu-like symptoms • Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy) Repeat measurements if • Baseline results are abnormal • Patient has symptoms of adverse reactions	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to "Section 7: Drug Interactions" on page 45 in "Treatment of Tuberculosis" at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf . Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC's Division of Tuberculosis "News and Updates" Web page at http://www.cdc.gov/tb/default.htm to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Adherence

Monitor patients for adherence to self-administered latent tuberculosis infection (LTBI) treatment regimens at least monthly throughout treatment.[34] It is difficult to identify who will and who will not be adherent.[35] If patients do not take medicine as directed, the effectiveness of the regimen decreases, and the patient will be at greater risk of progressing to disease in the future and of infecting others.

Monthly Assessment of Adherence

At each visit, the clinician should assess adherence by doing the following:

1. Ask patients how many doses they have missed since their last refill. If patients are asked, "Did you take all your pills last month?" the natural inclination is to say "yes" even if they did not.
2. Have patients bring their bottle of medicine to the refill appointment, and count how many pills are left.
3. If adherence problems are identified, include patients in the problem-solving process.
   a. Ask patients why they think that doses are missed and what could be done better: change the time of day, the location where they keep or take their pills, etc.
   b. Find out if there are barriers to obtaining refills in a timely manner that could be corrected.
   c. Review with patients what they believe is their risk of developing tuberculosis (TB) if medicine is not taken. Provide education again, as needed.
   d. Mutually agree upon a plan to improve adherence.
   e. Praise patients for cooperation.
4. If adherence seems to be good, praise patients.

For information on what to include in a patient education session, see the Patient Education section of the manual (15.1)

Directly Observed Therapy

Patients in the following high-risk groups are strongly recommended for directly observed therapy (DOT).

- DOT is mandatory for any intermittent regimen.
- DOT is strongly encouraged for those with the greatest risk for progression to tuberculosis (TB) disease:
  - Young children who are recent contacts to infectious cases.
  - Human immunodeficiency virus (HIV)-infected persons.

For more information, see the "Directly Observed Therapy/Videophone DOT" topic in the Case Management section of the manual (**8.51**).

For more information on adherence strategies for different developmental stages, see Appendix C in the New Jersey Medical School National Tuberculosis Center's *Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider* (New Jersey Medical School Global Tuberculosis Institute Web site; 2009) at http://www.umdnj.edu/ntbcweb/products/mgmtltbi.htm

Completion of Therapy

Determine whether and when therapy is completed based upon the total number of doses administered, not on the duration of therapy. When patients have had lapses in therapy but are still able to complete the recommended number of doses in the allotted time period, encourage them to complete therapy.

Assess patients who will not complete appropriate therapy within the time frame specified to determine whether or not to restart treatment. If the decision is made to retreat the patient, then **restart** the entire regimen and follow the recommended treatment plan of therapy. Specific factors to consider when determining whether to restart treatment include the following:

- Individual's risk for developing tuberculosis (TB) disease
- Total number of doses of latent tuberculosis infection (LTBI) treatment administered
- Time elapsed since the last dose of treatment for LTBI
- Patient adherence issues (previous attempts at completion, willingness to continue, etc.)

Give nonadherent patients who are at very high risk of developing TB disease every opportunity to complete treatment for LTBI. Consider these patients for intermittent therapy with directly observed therapy (DOT), and evaluate the use of incentives and enablers.[36]

Treatment of LTBI in contacts is considered a priority in TB control activities. Make every effort to assure completion of treatment in contacts.

All contacts who are being treated for infection should be seen face-to-face by a healthcare provider at least monthly. Incentives and enablers are recommended as aids to adherence, and the healthcare provider should educate the patient about TB, its treatment, and the signs of adverse drug effects at each patient encounter.[37]

Table 5 describes the duration of therapy and the number of doses that patients are required to take to complete therapy as well as the time frame within which the total number of doses must be administered for completion of therapy.

TABLE 5: RECOMMENDED REGIMENS FOR COMPLETION OF THERAPY[38]

Regimen	Age	Duration of Therapy	Number of Doses	Must be Administered Within
INH daily	Adult and child	9 months	270	12 months
INH daily	Adult	6 months	180	9 months
INH twice weekly	Adult and child	9 months	76	12 months
INH twice weekly	Adult	6 months	52	9 months
RIF daily	Adult	4 months	120	6 months
	Child	6 months	180	9 months
Definitions of abbreviations: INH = isoniazid; RIF = rifampin.				

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):26–27; CDC. Regimens. In: Chapter 6: treatment of LTBI. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: http://www.cdc.gov/tb/education/corecurr/index.htm. Accessed January 10, 2012.

Make every effort to encourage patients to adhere to the LTBI treatment regimen. However, if a patient has failed three attempts to complete treatment, no further effort may be merited. The healthcare provider should contact patients who interrupt therapy and are at high risk of developing TB disease (for example, contacts of patients with infectious TB, human immunodeficiency virus (HIV)-infected patients, or TB Class 4 patients) for reevaluation.[39]

Treatment in Special Situations

Treatment of latent tuberculosis infection (LTBI) in the following situations requires special consideration:

- Human immunodeficiency virus (HIV) infection
- Alcoholism

Human Immunodeficiency Virus and Latent Tuberculosis Infection

Treatment of latent tuberculosis infection (LTBI) in a person with human immunodeficiency virus (HIV) infection can be extremely complicated. Consultation is available through the WA State TB Services Medical Consultant 206-718-2664.

HIV infection is the strongest known risk factor for the progression of LTBI to tuberculosis (TB) disease. HIV-infected persons with LTBI are 100 times more likely to progress to TB disease than are those patients without HIV infection. Coinfected HIV and LTBI patients have a 7 to 10 percent *yearly* risk of developing TB disease. Patients with only LTBI have a 10 percent *lifetime* risk of developing TB disease.

High-risk contacts (less than 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For more information on time frames, see "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis" at http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

Resources

- CDC. "TB Guidelines: HIV/AIDS" (DTBE Web site; accessed February 2007). Available at: http://www.cdc.gov/tb/publications/guidelines/HIV_AIDS.htm .
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- CDC. "Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors" (*MMWR* 2000;49[No. 9]:185). Available at: http://www.cdc.gov/mmwr/PDF/wk/mm4909.pdf .

Alcoholism

Alcohol-Related Treatment Complications

Risk of drug-induced liver injury and nonadherence complicate health interventions for patients who are diagnosed with TB disease or latent tuberculosis infection (LTBI) and who also are known or suspected to have an alcohol use disorder, who drink heavily, or who regularly consume alcohol.

In several important ways related to tuberculosis and its treatment, alcohol consumption increases health risks and can complicate the treatment of patients.

- **Immunosuppression:** Persons who use alcohol may be at increased risk for acquiring or developing TB, but given the many other potential risk factors that commonly occur among such persons, alcohol use has been difficult to identify as a separate risk factor for TB.[40] However, studies have shown that "alcohol consumption is a major risk factor for infection with opportunistic bacterial, viral, fungal, and parasitic pathogens."[41]
- **Liver injury and death**: Drug-induced liver injury "may occur with all currently recommended regimens for the treatment of …LTBI".[42] In the treatment of TB disease, "the crucial efficacy of isoniazid, and particularly (INH), rifampin, warrants their use and retention, (RIF), and pyrazinamide (PZA), they should be used if at all possible, even in the face of preexisting liver disease."[43] However, it is not fully understood yet how antituberculosis medications cause drug-induced liver injury.[44] For persons taking isoniazid, an association of hepatitis was found with alcohol consumption, with rates being fourfold higher among persons consuming alcohol daily than among those who did not drink alcohol.[45] When a patient has hepatic disease, the risk of drug accumulation and drug-induced hepatitis is increased. However, with more frequent laboratory and clinical monitoring, isoniazid may be used in patients with stable hepatic disease. Transient asymptomatic hyperbilirubinemia may occur in patients taking rifampin or rifapentine, and more severe clinical hepatitis may also occur. Hepatitis is more common when rifampin is given with isoniazid than when rifampin is given alone or with drugs other than isoniazid.[46,47] Pyrazinamide has slightly lower rates of hepatotoxicity than isoniazid or rifampin, but pyrazinamide can cause liver injury that may be severe and prolonged.[48]
- To prevent and manage drug-induced liver injury, the American Thoracic Society recommends the following systematic steps: consideration of benefits and risks in selecting patients and regimens, careful and thorough staff and patient education, ready access to care, good communication between providers, and clinical and biochemical monitoring.[49], the most serious common adverse reaction, is defined as a serum aspartate aminotransferase (AST) level more than three times the upper limit of normal in the presence of symptoms or five times the upper limit of normal in the absence of symptoms.

- **Nonadherence to treatment:** Patients who do not complete LTBI treatment risk progression to TB disease, and those who do not complete treatment for TB disease risk relapse, development of drug-resistant TB, serious illness, and possible death. Barriers to adherence may be patient related, such as conflicting health beliefs, alcohol or drug dependence, or mental illness, or they may be system related, such as lack of transportation, inconvenient clinic hours, and lack of interpreters.[50] It is more difficult for patients who have an alcohol use disorder to adhere to therapy. In a prospective study of 224 patients, "noncompliance was significantly associated with homelessness and alcoholism."[51] In a study of 237 patients in the Russian Federation undergoing DOTS treatment for TB disease, "substance abuse was identified as the only factor that was strongly associated with non-adherence…These results suggest that DOTS programmes [sic] might be more likely to achieve TB control targets if they include interventions aimed at improving adherence by diagnosing and treating substance abuse concurrently with standard TB therapy."[52] DOTS programs that have explicitly offered substance abuse treatment have reported better outcomes that those that have not.[53] In South Carolina, joint treatment programs to treat patients with TB who have alcohol and substance abuse problems were used in conjunction with incentives, enablers, and a process of increasing restrictions (health department warnings, then court-ordered directly observed therapy, then involuntary confinement) as needed to address noncompliance. This combination of strategies was associated with an increase in overall completion of antituberculosis therapy and a decrease in new cases between 1986-1991.[54]

For more information, see "Tuberculosis Infection Control Program Model Policies for Chemical Dependency Treatment Agencies in Washington State," available at http://www.dshs.wa.gov/pdf/dbhr/certforms/TBPolicy.pdf

Pregnancy and Breastfeeding

Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progression to disease. Pregnant women should be targeted for testing only if they have a specific risk factor for LTBI or for progression of LTBI to disease.

Extensive use of INH during pregnancy has shown that, although it readily crosses the placental barrier, the drug is not teratogenic, even when given during the first four months of gestation. However, in the absence of risk factors (HIV infection or recent contact to infectious case), wait until after the woman has delivered to avoid administering unnecessary medication during pregnancy. There is potential for an increased risk of hepatotoxicity during pregnancy and the first 2-3 months of the post-partum period. Consider delaying treatment for LTBI until 2-3 months post-partum. Supplementation with 10-25mg/d of pyridoxine (vitamin B6) is recommended.

Breastfeeding is not contraindicated when the mother is being treated for LTBI. However, breastfeeding mothers taking INH and their nursing infants should receive supplemental

pyridoxine. Note that the amount of INH provided by breast milk is inadequate for treatment of the infant.[55]

Resources

- Red Book Plus 27th Edition, American Academy of Pediatrics, 2007. Available at http://www.aapredbook.org.

Resources and References

Resources

Whom to Treat

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Adherence

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  This module is entirely devoted to assessing and promoting adherence. It covers the many areas that need to be addressed, such as:

  - Case management: assigning responsibility to the healthcare worker
  - Communication and problem-solving skills
  - Education of the patient
  - Using interpreters when needed
  - Using incentives (rewards) and enablers (things that remove barriers for patients)
  - Using directly observed therapy (DOT)
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Confidentiality

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Introduction

Purpose

Use this section to do the following:

- Determine what information and which records should be treated with confidentiality;
- Identify state policy for maintaining patient confidentiality;
- Take measures to ensure TB patients' confidentiality; and
- Determine when it is permissible to share information for public health reasons.

The protection of private patient information is commonly referred to as confidentiality. Confidentiality involves the protection of information revealed during patient–healthcare worker encounters, including all written or electronic records of these encounters. Confidentiality is an essential issue in many different aspects of tuberculosis (TB) control. Healthcare workers need to be aware of confidentiality issues that are relevant to patient–healthcare worker encounters, as well as to the collection, management, and sharing of information gathered on TB patients.[1]

Policy

Healthcare workers should keep patient information in confidence and divulge it only with the permission of the patient, except as otherwise allowed by law.[2]

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction section of the manual (**1.16**).

Health Insurance Portability and Accountability Act (HIPAA)

Confidentiality of patient information has long been a requirement in the healthcare field and now has its own set of regulations, the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The new regulations protect the privacy of certain individually identifiable health data, referred to as protected health information (PHI). PHI is individually identifiable health information that is transmitted or maintained in any form or medium (e.g., electronic, paper, or oral), but excludes certain educational and employment records.

Centers for Disease Control and Prevention Guidance on HIPAA

The Centers for Disease Control and Prevention (CDC) published the report "HIPAA Privacy Rule and Public Health: Guidance from CDC and the US Department of Health and Human Services" (*MMWR* 2003;52 [S-2]:1–12 at http://www.cdc.gov/mmwr/preview/mmwrhtml/su5201a1.htm), to provide guidance in implementing the HIPAA requirements. In this report, the US Department of Health and Human Services (DHHS) recognized the importance of sharing PHI to accomplish essential public health objectives and to meet certain other societal needs (e.g., administration of justice and law enforcement).

Covered entities—which are health plans, healthcare clearinghouses, and healthcare providers who transmit health information in electronic form in connection with certain transactions—are permitted by the Privacy Rule to do the following:

- Share Public Health Information (PHI) for specified public health purposes. For example, covered entities may disclose PHI, without individual authorization, to a public health authority legally authorized to collect or receive the information for the purpose of preventing or controlling disease, injury, or disability.
- Make disclosures that are required by other laws, including laws that require disclosures for public health purposes.[3]

Revised Code of Washington (RCW)

- RCW 70.02- Medical Records- Health Care Access Information and Disclosure
  http://apps.leg.wa.gov/RCW/default.aspx?cite=70.02&full=true
- RCW 42.56 – Public Records
  http://apps.leg.wa.gov/RCW/default.aspx?cite=42.56&full=true

National Guidelines

The following guidelines for protecting tuberculosis (TB) patients' confidentiality are adapted from the National Tuberculosis Controllers Association's (NTCA's) and Centers for Disease Control and Prevention's (CDC's) "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC" (*MMWR* 2005;54[No. RR-15]).

TABLE 1: HOW TO PROTECT CONFIDENTIALITY

Conducting All Activities	• Make every attempt to ensure patient confidentiality.
Training	• Participate in training on maintaining confidentiality and obtaining informed consent in accordance with local/state laws.
Interviewing Patients	• Interview the tuberculosis (TB) patient in a private setting. • Inform the patient about confidentiality rights. • Explain to a human immunodeficiency virus (HIV)-infected patient that HIV status will be kept confidential (WAC 246-101-120). • Consult with the patient to identify boundaries for confidentiality and obtain oral consent for any breaches in confidentiality. • If written consent is required, present the consent form to the patient in an appropriate manner, and retain a copy in the patient's medical record. If consent is refused, the TB program should develop a plan of action.
Conducting Site Investigations	• Plan site investigation procedures in advance of any visit, in consultation with and with the consent of the index patient, if possible. • Obtain agreement to maintain confidentiality from any site personnel who receive information about the identity of the index patient.
Communicating with the Press	• Maintain confidentiality in communications with the press.
Breaching Confidentiality	• Breach confidentiality only with approval of TB Services administrators and with the consent of the TB patient, when possible.

Resources and References

Resources

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Interjurisdictional Transfer Notifications

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Forms Used in this Section

- Interjurisdictional Transfer Notification
- Interjurisdictional Transfer Notification Follow-Up

Introduction

Purpose

Use this section to do the following:

- Notify public health agency staff in another jurisdiction that a person is moving (or has moved) to their jurisdiction who is a
  - Verified or suspected case of tuberculosis (TB) disease;
  - High-priority contact to a smear-positive Class 3 or Class 5 pulmonary case, contact to a smear-negative Class 3 pulmonary case, or contact to a highly suspect Class 5 pulmonary case;
  - Documented convertor who has initiated treatment for latent tuberculosis infection (LTBI);
  - Class 2 or Class 4 patient who has initiated treatment for LTBI; or
  - Close associate to a Class 3 index case with clinical presentation consistent with recently acquired disease in a source-case investigation or close associate to a child with LTBI in a source-case investigation.
- Follow up on notifications
- Make CURE-TB referrals for TB patients and contacts who move between the United States and Mexico.

Enroll mobile TB patients in the TBNet tracking and referral service. Making sure that TB patients complete their evaluation and treatment is a critical element of TB control.[1] Some patients receiving treatment for TB disease in the United States move from one jurisdiction to another before completing treatment. Notifying the receiving local and/or state jurisdiction of a patient's impending arrival will prevent care from being interrupted and improve treatment outcome.

The term interjurisdictional transfer notification refers to a referral or follow-up report. Before the patient moves, or as soon as it becomes apparent that a patient has moved, the referring jurisdiction provides a referral to the receiving jurisdiction. After the patient has moved, the receiving jurisdiction then provides the referring jurisdiction with a follow-up report.

Policy

The Washington State TB Services is responsible for coordination of transfer notifications between states and other local jurisdictions within the state. The local public health jurisdiction should notify the state department of health when a patient plans or requests to transfer to another jurisdiction. The receiving and referring jurisdictions should stay in communication until final dispensation of the patient is known.

When to Initiate a Notification

For a definition of tuberculosis (TB) patient classifications, see the "Tuberculosis Classification System" topic in the Surveillance Section (2.7)

TABLE 1: INTERJURISDICTIONAL TRANSFER NOTIFICATIONS AND FOLLOW-UPS[2]

Referral Type	When to Initiate	Notes
Verified and suspected cases of tuberculosis (TB) disease	When notified that a Class 3 or 5 patient is moving or has moved from the area for 30 days or more	May also initiate to coordinate directly observed therapy (DOT) while patient is visiting another area.
Contacts	After identifying a: • High-priority contact to a smear-positive Class 3 or Class 5 pulmonary case • Contact to a smear-negative Class 3 pulmonary case • Contact to a highly suspect Class 5 pulmonary case	Send individual referrals for each contact.
Latent TB Infection (LTBI) converters	When notified that a documented convertor who has initiated treatment is moving or has moved from the area for 30 days or more	
LTBI reactors	When notified that a Class 2 or 4 patient who has initiated treatment is moving or has moved from the area for 30 days or more	
Source case investigation for TB disease	After identifying a close associate to a Class 3 index case with clinical presentation consistent with recently acquired disease	Use primarily for associates to children under 5 years of age with TB disease. A younger age cut-off may be advisable because the focus would be on more recent transmission.[3]

Referral Type	When to Initiate	Notes
Source case investigation for LTBI	After identifying a close associate to a child with LTBI	Use primarily for associates to children under 2 years of age with LTBI.[4]
Follow-Up Type	**When to Initiate**	**Notes**
Final disposition	When final status and/or outcome is known	

Source: NTCA. *Interjurisdictional Tuberculosis (TB) Notification—National Tuberculosis Controllers Association Recommendations.* Smyrna, GA: March 2002:1–5.

How to Issue an Interjurisdictional Notification

- **Outside the United States:** Contact the Washington State TB Services 360-236-3443 The CDC has a process for international notification, available at http://cdc.gov/tb/programs/international/default.htm
- **Inside the United States (within the state or between states):** See Table 2.

An interjurisdictional tuberculosis (TB) notification system has been set up by the National Tuberculosis Controllers Association (NTCA) to facilitate and standardize communication between states. This system will enhance continuity and completeness of care, and improve outcome evaluation of verified cases.[5]

TABLE 2: REFERRALS IN THE UNITED STATES[6]

Action	Transfers Within Washington	Transfers Between States
Make a referral	The LHJ from which the patient is transferring should do the following as soon as possible: • Complete an Interjurisdictional Tuberculosis Notification form and mail/fax to WA State DOH TB Services • Print a copy of the Reported Verified Case of TB (RVCT) form from PHIMS TB for your records • In PHIMS TB, transfer patient to available LHJ • Call the patient's medical provider and arrange for transfer of the patient's records to the receiving physician (or to the jurisdiction receiving the patient if no receiving physician is designated)	The State and Local Health Jurisdiction from which the patient is transferring should do the following as soon as possible: • Complete an Interjurisdictional Tuberculosis Notification form and mail/fax to WA State DOH TB Services • Print a copy of the Reported Verified Case of TB (RVCT) form from PHIMS TB for your records
Give the patient records	The LHJ from which the patient is transferring should provide the patient a copy of the treatment records	The LHJ from which the patient is transferring should provide the patient a copy of the referral and treatment records
Follow up on referrals	Complete Interjurisdictional TB Notification Follow-Up †	Complete Interjurisdictional TB Notification Follow-Up †

* The NTCA's "Interjurisdictional Tuberculosis Notification"

† The NTCA's "Interjurisdictional TB Notification Follow-Up"

Source: NTCA. *Interjurisdictional Tuberculosis (TB) Notification–National Tuberculosis Controllers Association Recommendations.* Smyrna, GA: March 2002:1–5.

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Patient Education

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Forms Used in this Section
• No Forms are Used in This Section

Introduction

Purpose

Use this section to do the following:

- Determine what information to cover in education sessions
- Educate patients about tuberculosis (TB)
- Educate patients about latent TB infection (LTBI)
- Identify which forms to use to document education efforts

An important part of helping patients take their medicine is educating them about TB. This means talking to them about the cause of TB, the way TB is spread, how TB is diagnosed, and their specific treatment plan.[1] Patients cannot be expected to adhere to treatment recommendations if they are not educated about TB and how it is treated, and patients who understand these concepts are more likely to adhere to treatment.

Patients with LTBI need to understand that they are infected with TB, that they may have specific risks for progressing to TB disease, and that they can take precautions to protect themselves, their family, and their friends. Patients with TB disease need to understand the seriousness of the disease and why it is important to adhere to treatment. In order to prevent relapse and drug resistance, clinicians must prescribe an adequate regimen and make sure that patients adhere to treatment.[2] To ensure completion of treatment, the public health department should thoroughly educate the patient, monitor the patient's adherence, and use incentives and enablers.[3,4,5]

General Guidelines

TABLE 1: GUIDELINES FOR THE EDUCATIONAL PROCESS

When Educating Tuberculosis (TB) Patients	
Do	**Don't**
• Find out what patients know and believe about TB. Reinforce and provide correct TB information, and disabuse them of any misconceptions. • Use good skills to interview and influence patients, and to problem solve. • Go through the educational material with patients. Use language appropriate to their level of understanding. If necessary, use an interpreter.	• Flood patients with information about TB and its effects without allowing them to participate in the discussion. • Hand out pamphlets and brochures to patients without going through the materials with them.

Education Topics

During the initial assessment, directly observed therapy (DOT)/Videophone DOT appointments, and monthly monitoring, educate the patient as needed on the topics that follow.

Language and Comprehension Barriers

In the initial assessment, assess for and address any potential language and comprehension barriers.

1. Assess the patient's ability to speak and understand instructions, including potential barriers, such as not speaking English as primary language, deafness, speech deficit, or learning disability.
2. Assess literacy in the patient's primary language.
3. Provide all instructions and communications in the appropriate language.
4. Use interpreters, visuals, or other educational methods to promote understanding.
5. Provide educational materials appropriate to the patient's language and reading level.
6. Make referrals to an appropriate service and notify it of any language and comprehension concerns.

For more information on cultural sensitivity, refer to the *Participant's Workbook* for Session 4: "Working with Culturally Diverse Populations" in the *Directly Observed Therapy Training Curriculum for TB Control Programs* (Curry International Tuberculosis Center Web site; 2003) at http://www.currytbcenter.ucsf.edu/catalogue/epub/index.cfm?tableName=DOTE.

For assistance with language issues, see the *Language Services Resource Guide for Health Care Providers* (The National Health Law Program Web site; 2006) at http://www.healthlaw.org/images/pubs/ResourceGuideFinal.pdf

TB PhotoVoice assists individuals impacted by TB to document their own health realities by taking photographs of the people, places and systems that both positively and negatively affect the care and treatment of their tuberculosis. For more information please visit http://tbphotovoice.org

Medical Diagnosis

In the initial interviews with the patient, provide information about TB and the patient's treatment plan. During DOT appointments and monthly monitoring, confirm and reinforce the patient's understanding of these topics.

1. Discuss the difference between TB disease and TB infection.
2. Explain the signs and symptoms of TB, how TB is transmitted, prevention activities, and treatment.
3. Explain that TB is both treatable and preventable.
4. Explain the importance of completion of treatment.
5. Discuss diagnostic procedures used to make diagnosis of TB, such as chest radiography, sputum microscopy, and tuberculin skin testing. Stress the importance of testing and follow-up.
6. Discuss the current medical treatment plan and rationale. Have the patient sign the treatment plan and a DOT agreement.
7. Explain the need for regular medical monitoring and follow-up during the disease process. Discuss how treatment will be monitored (i.e., sputum, blood tests, vision screening, weight check, etc.). Encourage the patient to be an active participant in care and treatment.
8. Discuss the roles of the patient (engage in treatment), the health department (case management, monitoring, contact tracing, and supervision of treatment), and the medical provider (treatment and monitoring). Encourage the patient to contact the case manager for issues and problems that arise during treatment.

9. Explain the risk of treatment relapse or failure and the need to complete treatment to prevent relapse.
10. Explain the signs and symptoms of possible relapse or failure, and encourage the patient to report them immediately to the case manager.

Contact Investigation

When a contact investigation is necessary, educate the index patient about the process and confidentiality.

1. Discuss the contact investigation process.
2. Reinforce the confidentiality of investigation, but warn the patient of the potential for contacts to guess the patient's identity.

For more information see Effective TB Interviewing for Contact Investigation: Self Study Modules:

http://www.cdc.gov/tb/publications/guidestoolkits/Interviewing/default.htm

Isolation

If isolation is necessary, educate the patient about how to take proper precautions.

1. Explain isolation precautions and restrictions, if appropriate. Have the patient sign an isolation agreement.
2. Explain the behavior changes needed for infection control. Discuss permitted and prohibited activities, limiting and excluding visitors, covering the mouth and nose when coughing and sneezing, and using a mask.
3. Explain the home environmental changes needed for infection control. Discuss ventilation and sunlight. Explain how to dispose of items soiled with potentially infectious material.
4. Discuss the requirements for release from isolation. Advise the patient that clearance is contingent upon clinical condition and continued compliance with the treatment regimen.

Side Effects and Adverse Reactions

Educate all patients on antituberculosis medications about the medications' potential side effects and adverse reactions.

1. Explain the names, dosages, and rationale for the drug treatment plan as well as the importance of treatment.
2. Explain the common side effects and methods to improve symptoms.
3. Explain signs and symptoms of drug toxicity.
4. Direct the patient on what actions to take if side effects or signs and symptoms of toxicity appear.
5. Explain potential effects of alcohol and/or drug use on treatment and the increased risk for side effects and toxicity.

For more information on side effects and adverse reactions, see the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section (**5.19**).

Adherence

If a patient has the potential for not adhering to the treatment plan, educate the patient about the importance of treatment, the patient's responsibilities during treatment, and the consequences of nonadherence.

1. Explain the importance of treatment and follow-up for active TB.
2. Explain the importance of regular monitoring visits.
3. Discuss the treatment plan and expectations. Advise the patient on the patient's responsibilities and expected behavior regarding treatment compliance and follow-up activities. Have the patient sign the treatment plan and a DOT agreement.
4. Advise the patient on laws regarding TB disease and isolation.

Patient Education Materials

The Centers for Disease Control and Prevention (CDC) offers the following patient education materials online (as of January 2007).

- *Get the Facts About TB Disease*
  http://www.cdc.gov/tb/publications/pamphlets/getthefacts_eng.htm
- *Protect Your Friends and Family from TB: The TB Contact Investigation*
  http://www.cdc.gov/tb/publications/pamphlets/TB_contact_investigation.pdf
- *Questions and Answers About TB*
  http://www.cdc.gov/tb/publications/faqs/default.htm
- *Staying on Track with TB Medicine*
  http://www.cdc.gov/tb/publications/pamphlets/TB_trtmnt.pdf
- *Stop TB*
  http://www.cdc.gov/tb/publications/Posters/stoptb.htm
- *Tuberculosis: General Information*
  http://www.cdc.gov/tb/publications/factsheets/general.htm
- *What You Need to Know About TB Infection*
  http://www.cdc.gov/tb/publications/pamphlets/TB_infection.pdf
- *What You Need to Know About the TB Skin Test*
  http://www.cdc.gov/tb/publications/pamphlets/TB_skin_test.pdf

For other sources of patient education materials see all four Regional Training and Medical Consultation Consortium websites:

- Curry International Tuberculosis Center (http://www.currytbcenter.ucsf.edu/)
- Heartland National TB Center (http://www.heartlandntbc.org/)
- Northeastern Regional Training and Medical Consultation (http://www.umdnj.edu/globaltb/rtmcc.htm)
- Southeastern National TB Center (http://sntc.medicine.ufl.edu/)

Resources and References

Resources

Patient Education Information for Healthcare Workers

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (*MMWR* 2000;49[No. RR-6]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf ; and Updates available at: http://www.cdc.gov/tb/publications/reportsarticles/mmwr/default.htm .
- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm .
    - Module 9: "Patient Adherence to Tuberculosis Treatment." Available at: http://www.cdc.gov/tb/education/ssmodules/module9/ss9contents.htm .
    - Module 4: "Treatment of Tuberculosis Infection and Disease, Adherence to Treatment." Available at: http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf .
- CDC. *TB Elimination: Now Is the Time! 2007* (Division of Tuberculosis Elimination Web site; 2007). Available at: http://www.cdc.gov/tb/publications/pamphlets/nowisthetime/default.htm .

Patient Education Materials for Patients

- CDC. *TB Education and Training Resources* [TB Education and Training Resources Web site]. Available at: http://www.findtbresources.org/scripts/index.cfm .
- CDC, Division of Tuberculosis Elimination. *Education and Training Materials* [Division of Tuberculosis Elimination Web site]. Available at: http://www.cdc.gov/tb/education/default.htm .
- Minnesota Department of Health. *Tuberculosis: Patient Education Materials* [Minnesota Department of Health Web site]. Available at: http://www.health.state.mn.us/divs/idepc/diseases/tb/education.html.
- University of Washington Harborview Medical Center. *Patient Education Resources: All Languages* [EthnoMed Web site]. Available at: http://ethnomed.org/patient-education/tuberculosis .

References

[1] CDC. Module 4: treatment of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:12. Available at: http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf . Accessed January 10, 2012.

[2] CDC. Module 4: treatment of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:12. Available at: http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf . Accessed January 10, 2012.

[3] CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):38–39.

[4] National Tuberculosis Controllers Association, National Tuberculosis Nurse Consultant Coalition. *Tuberculosis Nursing: A Comprehensive Guide to Patient Care.* Atlanta, GA: 1997:64, 69, 74.

[5] CDC. Module 9: patient adherence to tuberculosis treatment. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:9–11. Available at: http://www.cdc.gov/tb/education/ssmodules/module9/ss9contents.htm. Accessed January 10, 2012.

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FORMS

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Authorization for Care Coordination (PHSKC)

- To request this document in WORD, email **tbservices@doh.wa.gov**

Authorization for Disclosure of Protected Health Information (PHSKC)

- To request this document in WORD, email **tbservices@doh.wa.gov**

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Binational Card Sample

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Case Initial Assessment/Education (Clark/Skamania Counties)

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Chart Audit Tool

- To request this document in WORD, email **tbservices@doh.wa.gov**

Clinic Record (SHD)

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- To request this document in WORD, email **tbservices@doh.wa.gov**

Contact Investigation Instructions

- To request this document in WORD, email **tbservices@doh.wa.gov**

Cure TB Brochure (CureTB)

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Directly Observed Therapy Agreement (PHSKC)

- To request this document in WORD, email **tbservices@doh.wa.gov**

Direct Observed Therapy Agreement (Virginia)

Directly Observed Therapy Audit Tool

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Directly Observed Therapy Log (Virginia)

Do Not Board (DNB) Protocol

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Drug Interview Sheet (SHD)

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- To request this document in WORD, email **tbservices@doh.wa.gov**

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Health Advisory (Clark/Cowlitz/Skamania/Wahkiakum Counties)

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- To request this document in WORD, email **tbservices@doh.wa.gov**

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- To request this document in WORD, email **tbservices@doh.wa.gov**

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- To request this document in WORD, email **tbservices@doh.wa.gov**

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Personal Safety Guide for Field Workers (Chelan-Douglas County)

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Policies and Procedures/Inventory (TB Program Videophones)

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Policies and Procedures/Requests (TB Program Videophones)

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Protocols and Standing Orders (SHD)

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Public Health Directive (PHSKC)

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Tuberculosis Control Referral Form (SHD)

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Videophone DOT (TPCHD)

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Videophone Directly Observed Therapy (DOT) Consent

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Washington State Tuberculosis Staffing Model

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Glossary

acid-fast bacilli (AFB): Microorganisms that are distinguished by their retention of specific stains even after being rinsed with an acid solution. An AFB examination involves microscopic examination of a stained smear of a patient specimen (usually sputum) to determine if mycobacteria are present. The relative concentration of AFB per unit area on a slide (the smear grade) is associated with infectiousness. A presumptive diagnosis of pulmonary TB can be made with a positive AFB sputum smear result. However, approximately 50% of patients with TB disease of the lungs have negative AFB sputum smear results. The majority of AFB in patient specimens are mycobacteria, including species other than *Mycobacterium tuberculosis* complex. A positive nucleic acid amplification or culture result is needed for confirmation of *M. tuberculosis* complex.

administrative controls: Managerial measures that reduce the risk for exposure to persons who might have TB disease. Examples include coordinating efforts with the local or state health department; conducting a TB risk assessment for the setting; developing and instituting a written TB infection control plan to ensure prompt detection, airborne infection isolation, and treatment of persons with suspected or confirmed TB disease; and screening and evaluating healthcare workers who are at risk for TB disease or who might be exposed to *M. tuberculosis.*

air change rate: Ratio of the airflow in volume units per hour to the volume of the space under consideration in identical volume units, usually expressed in air changes per hour (ACH).

air changes per hour (ACH): Air change rate expressed as the number of air exchange units per hour.

airborne infection isolation (AII) precautions: The isolation of patients infected with organisms spread through airborne droplet nuclei 1–5 μm in diameter. This isolation area receives substantial air changes per hour (ACH) (≥12 ACH for new construction since 2001 and ≥6 ACH for construction before 2001) and is under negative pressure (i.e., the direction of the air flow is from the outside adjacent space [e.g., the corridor] into the room). The air in an AII room is preferably exhausted to the outside but can be recirculated if the return air is filtered through a high efficiency particulate filter.

airborne infection isolation room (AII room): A room designed to maintain AII. Formerly called negative pressure isolation room, an AII room is a single-occupancy patient-care

room used to isolate persons with suspected or confirmed infectious TB disease. Environmental factors are controlled in AII rooms to minimize the transmission of infectious agents that are usually spread from person-to-person by droplet nuclei associated with coughing or aerosolization of contaminated fluids. AII rooms should provide negative pressure in the room (so that air flows under the door gap into the room), have an air flow rate of 6–12 air changes per hour, and direct exhaust of air from the room to the outside of the building or recirculation of air through a high efficiency particulate filter.

anergy: A condition in which a person has a diminished ability to exhibit delayed T-cell hypersensitivity to antigens because of a condition or situation resulting in altered immune function. Skin tests for anergy (i.e., control antigens) have poor predictive value and are not recommended.

asymptomatic: Neither causing nor exhibiting signs or symptoms of disease.

bacille Calmette-Guérin (BCG): Vaccines for tuberculosis named after the French scientists Calmette and Guérin. The vaccines are effective in preventing disseminated and meningeal TB disease in infants and young children. They might have approximately 50% efficacy for preventing smear-diagnosed pulmonary TB in adults. They are used in multiple countries where TB disease is endemic. Centers for Disease Control and Prevention. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR 2005;54 (No. RR-12):[inclusive page numbers].

baseline tuberculosis screening: Screening healthcare workers (HCWs) for latent TB infection and TB disease at the beginning of employment. TB screening documented tuberculin skin tests (TSTs) or blood assays for *M. tuberculosis* (BAMTs) for those with previous negative test results for *M. tuberculosis* infection. The TST or BAMT is administered at the beginning of employment to newly hired HCWs. If the TST method is used for HCWs who have not had a documented negative test result for *M. tuberculosis* during the preceding 12 months, the baseline TST result should be obtained by using the two-step method. BAMT baseline testing does not need the two-step method.

blood assay for Mycobacterium tuberculosis (BAMT): A general term to refer to recently developed *in vitro* diagnostic tests that assess for the presence of infection with *M. tuberculosis*. This term includes, but is not limited to, interferon gamma (IFN-γ) release assays (IGRA).

boosting phenomenon: A phenomenon in which people who are skin tested many years after becoming infected with M. tuberculosis may have a negative reaction to an initial TST, followed by a positive reaction to a TST given up to a year later; this happens because the first TST boosts the immune response. Two-step testing is used in TB testing programs to tell the difference between boosted reactions and reactions caused by

recent infection (see two-step testing) http://www.cdc.gov/tb/education/ssmodules/pdfs/Glossary.pdf. Boosting does not pertain to IGRAs.

bronchoscopy: A procedure for examining the lower respiratory tract in which the end of an endoscopic instrument is inserted through the mouth or nose (or tracheotomy) and into the respiratory tree. Bronchoscopy can be used to obtain diagnostic specimens. Bronchoscopy also creates a high risk for *M. tuberculosis* transmission to healthcare workers (HCWs) if it is performed on an untreated patient who has TB disease (even if the patient has negative acid-fast bacilli smear results) because it is a cough-inducing procedure.

case: A particular instance of a disease (e.g., TB), referring only to the disease, not to the person with the disease. A case is detected, documented, and reported.

case management: A system in which a specific health department employee is assigned primary responsibility for the patient, systematic regular review of patient progress is conducted, and plans are made to address any barriers to adherence.

cavity (pulmonary): A hole in the lung parenchyma, usually not involving the pleural space. Although a lung cavity can develop from multiple causes, and its appearance is similar regardless of its cause, in pulmonary TB disease, cavitation results from the destruction of pulmonary tissue by direct bacterial invasion and an immune interaction triggered by *M. tuberculosis*. A TB cavity substantial enough to see with a normal chest radiograph predicts infectiousness.

chest x-ray: See **radiography**.

clinical examination: A physical evaluation of the clinical status of a patient by a physician or equivalent practitioner.

cluster (TB): A group of patients with latent TB infection or TB disease that are linked by epidemiologic, location, or genotyping data. Two or more tuberculin skin test conversions within a short period can be a cluster of TB and might suggest transmission within the setting. A genotyping cluster is 2 or more cases with isolates that have an identical genotyping pattern.

confirmed TB: A diagnosis of TB disease based on positive cultures for *M. tuberculosis.* However, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture. Positive cultures for *M. tuberculosis* confirm the diagnosis of TB; however, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture. Culture examinations should be done on all specimens, regardless of acid-fast bacilli smear results.

contact: A person who has been exposed to *M. tuberculosis* infection by sharing air space with a person with infectious TB.

contact investigation: Procedures that occur when a case of infectious TB is identified, including finding persons (contacts) exposed to the case, testing and evaluation of contacts to identify latent TB infection or TB disease, and treatment of these persons, as indicated.

contagious: See **infectious**.

conversion: A change in the result of a test for *M. tuberculosis* infection that is interpreted to indicate a change from being uninfected to infected. With the tuberculin skin test, an increase of more than 10 mm in induration size during a maximum of 2 years is defined as a conversion. If an interferon gamma release assay (IGRA) is used for testing, a conversion is a change from negative to positive within 2 years without any consideration of the magnitude of the change in TB response. A conversion is presumptive evidence of new *M. tuberculosis* infection and poses an increased risk for progression to TB disease. The term is applied to contacts only when previous test results are available. A change in tuberculin status during the window period is not necessarily consistent with this definition.

conversion rate: The percentage of a population with a converted test result (tuberculin skin test or blood assay for *M. tuberculosis*) for *M. tuberculosis* within a specified period. This is calculated by dividing the number of conversions among eligible healthcare workers (HCWs) or contacts in the setting in a specified period (numerator) by the number of HCWs or contacts who received tests in the setting over the same period (denominator) multiplied by 100.

culture: Growth of microorganisms in the laboratory performed for detection and identification in sputum or other body fluids and tissues. This test usually takes 2 to 4 weeks for mycobacteria to grow (2 to 4 days for most other bacteria).

delayed-type hypersensitivity (DTH): Cell-mediated inflammatory reaction to an antigen, which is recognized by the immune system usually because of previous exposure to the same antigen or similar ones. Cell-mediated reactions are contrasted with an antibody (or humoral) response. DTH typically peaks at 48–72 hours after exposure to the antigen.

deoxyribonucleic acid (DNA) genotyping: A clinical laboratory technique used to distinguish between different strains *of M. tuberculosis* and to help assess the likelihood of TB transmission.

directly observed therapy (DOT): An adherence-enhancing strategy in which a healthcare worker or other trained person watches a patient swallow each dose of medication and

is accountable to the public health system. A live video camera confirmation of ingestion of medicine of carefully selected patients (e.g., stable and compliant) constitutes DOT. DOT is the standard of care for all patients with TB disease and is a preferred option for patients treated for latent TB infection.

disseminated TB: See **miliary TB**.

droplet nuclei: Microscopic particles produced when a person coughs, sneezes, shouts, or sings. These particles can remain suspended in the air for prolonged periods and can be carried on normal air currents in a room and beyond to adjacent spaces or areas receiving exhaust air.

drug susceptibility test: A laboratory determination to assess whether an *M. tuberculosis* complex isolate is susceptible or resistant to anti-TB drugs that are added to mycobacterial growth medium or are detected genetically. The results predict whether a specific drug is likely to be effective in treating TB disease caused by that isolate.

enabler: A practical item given to a patient for making adherence (e.g., to treatment or to clinic appointments) easier.

environmental controls: Physical or mechanical measures (as opposed to administrative control measures) used to reduce the risk for transmission of *M. tuberculosis* by preventing the spread and reducing the concentration of infectious droplet nuclei in ambient air. Examples include ventilation, filtration, ultraviolet lamps, airborne infection isolation rooms, and local exhaust ventilation devices.

epidemiologic cluster: A closely grouped series of cases in time or place.

erythema: Abnormal redness of the skin. Erythema may develop around a tuberculin skin test (TST) site, but should not be read as part of the TST result.

evaluation of contacts: A process for diagnostic and public health evaluation of contacts that includes an initial encounter and, if needed, a medical evaluation. The decision about whether and when to evaluate a contact is based upon whether the contact is high, medium, or low priority. The initial encounter is a face-to-face meeting that allows the public-health worker to assess the overall health of the contact, administer a tuberculin skin test or IGRA and schedule further evaluation. Based on information from the initial encounter, the contact's priority may be reassessed and decisions made on whether to conduct a medical evaluation and which diagnostic tests to include in that evaluation. The medical evaluation is complete when the contact's status with respect to *M. tuberculosis* infection or TB disease has been determined.

exposure: The condition of being subjected to something (e.g., an infectious agent) that could have a harmful effect. A person exposed to *M. tuberculosis* does not necessarily

become infected. Much of the work in a TB contact investigation is dedicated to learning who was exposed and, of these, who became infected.

exposure incident: A situation in which persons (e.g., household, healthcare workers, visitors, and inmates) have been exposed to a person with suspected or confirmed infectious TB disease (or to air containing *M. tuberculosis*) without the benefit of effective infection control measures.

exposure period: The coincident period when a contact shared the same air space as a person with TB during the infectious period.

exposure site: A location that the index patient visited during the infectious period (e.g., school, bar, bus, or residence).

extrapulmonary TB: TB disease in any part of the body other than the lungs (e.g., the kidney, spine, bone, or lymph nodes). The presence of extrapulmonary disease does not exclude pulmonary TB disease.

false-negative tuberculin skin test (TST) or interferon gamma release assay (IGRA) result: A TST or IGRA result that is interpreted as negative in a person who is actually infected with *M. tuberculosis*.

false-positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) result: A TST or IGRA result that is interpreted as positive in a person who is not actually infected with *M. tuberculosis*. A false-positive TST result is more likely to occur in persons who have been vaccinated with bacille Calmette-Guérin or who are infected with nontuberculous mycobacteria. The IGRA ignores previous bacille Calmette-Guérin vaccines.

field investigation: A field investigation includes visiting the patient's home or shelter, workplace or school, and other places where the patient said he or she spent time while infectious. The field investigation should be done even if the patient interview has already been conducted. The purpose of the field investigation is to identify contacts and evaluate the environmental characteristics of the place or places in which exposure may have occurred.

fit check: A procedure performed after every respirator is donned to check for proper seal of the respirator. Also called “user-seal check.”

fit test: The use of a protocol to qualitatively or quantitatively evaluate the fit of a respirator on a person.

genotype: The deoxyribonucleic acid (DNA) pattern of *M. tuberculosis* used to discriminate among different strains.

healthcare workers (HCWs): All paid and unpaid persons working in healthcare settings.

hemoptysis: The expectoration or coughing up of blood or blood-tinged sputum—one of the symptoms of pulmonary TB disease. Hemoptysis can also be observed in other pulmonary conditions (e.g., lung cancer), although is most common in bronchitis and pneumonia.

high efficiency particulate air (HEPA) filter: A portable or stationary filter that is certified to remove more than 99.97% of particles 0.3 *µ*m in size, including *M. tuberculosis*-containing droplet nuclei. Use of HEPA filters in building ventilation systems requires expertise in installation and maintenance.

human immunodeficiency virus (**HIV) infection:** Infection with the virus that causes acquired immunodeficiency syndrome (AIDS). A person with both latent TB infection and HIV infection is at high risk for developing TB disease.

hypersensitivity: A state in which the body reacts with an exaggerated immune response to a foreign substance. Hypersensitivity reactions are classified as immediate or delayed, types I and IV, respectively. See **delayed-type hypersensitivity**.

immunocompromised and immunosuppressed: Conditions in which at least part of the immune system is functioning at less than normal capacity. According to some style experts, “immunocompromised” (e.g., diabetes) is the broader term, and “immunosuppressed” (e.g., steroids) is restricted to conditions with iatrogenic causes, including treatments for another condition. Some immunocompromised conditions increase the likelihood that *M. tuberculosis* infection will progress to TB disease. Certain conditions also make TB disease or infection from *M. tuberculosis* more difficult to diagnose because manifestations of TB disease differ and tests for infection rely on an intact immune system.

incentive: A gift given to patients to encourage or acknowledge their adherence to treatment.

incidence: The number of new events or cases of disease that develop during a specified period.

index (TB): The first case or patient with TB disease that comes to attention as an indicator of a potential public health problem.

induration: The firmness in the skin test reaction produced by immune-cell infiltration in response to the tuberculin antigen that was introduced into the skin during a tuberculin skin test. Induration is measured transversely by palpation, and the result is recorded in millimeters. The measurement is compared with guidelines to determine whether the test result is classified as positive or negative.

infection control program (TB): A program designed to control transmission of *M. tuberculosis* through early detection, isolation, and treatment of persons with infectious TB. A hierarchy of control measures are used, including 1) administrative controls to reduce the risk for exposure to persons with infectious TB disease and screening for healthcare workers (HCWs) for latent TB infection and TB disease, 2) environmental controls to prevent the spread and reduce the concentration of infectious droplet nuclei in the air, and 3) respiratory protection in areas where the risk for exposure to *M. tuberculosis* is high (e.g., airborne infection isolation rooms). A TB infection control plan should include surveillance of HCWs who have unprotected high-risk exposure to TB patients or their environment of care.

infection: A condition in which microorganisms have entered the body and typically have elicited immune responses. *M. tuberculosis* infection might progress to TB disease. The expression "*M. tuberculosis* infection" includes both latent infection and TB disease. Latent *M. tuberculosis* infection or latent tuberculosis infection (LTBI) is an asymptomatic condition that follows the initial infection; the infection is still present but is dormant (and believed not to be currently progressive or invasive). TB disease is determined by finding anatomic changes caused by advancing infection (e.g., shadows from infiltrates on a chest radiograph) or by noting symptoms (e.g., malaise, feverishness, or cough), and typically by both. Positive culture results for *M. tuberculosis* complex typically are interpreted as both an indication of TB disease and its confirmation, but infecting organisms can be obtained from patients who have no other evidence of disease.

infectious: Refers either to TB disease of the lungs or throat which has the potential to cause transmission to other persons, or to the patient who has TB disease.

infectious droplet nuclei: Droplet nuclei produced by an infectious TB patient that can carry tubercle bacteria and be inhaled by others. Although usually produced from patients with pulmonary TB through coughing, infectious droplet nuclei can also be produced by aerosol-generating procedures. Droplet nuclei can be generated during an autopsy.

infectious period: The period during which a person with TB disease might have transmitted *M. tuberculosis* organisms to others. For patients with positive acid-fast bacilli (AFB) sputum smear results, the infectious period begins 3 months before the collection date of the first positive smear result or the symptom onset date (whichever is earlier) and ends when the patient is placed into airborne infection isolation (AII) or the date of collection for the first of consistently negative smear results. For patients with negative AFB sputum smear results, the infectious period extends from 1 month before the symptom onset date and ends when the patient is placed into AII (whichever was earlier).

interferon-γ (gamma) release assay (IGRA): A blood test that detects cell-mediated immune response to this cytokine.

laryngeal TB: A form of TB disease that involves the larynx and can be highly infectious.

latent TB infection (LTBI): See **infection**.

Mantoux method: A skin test performed by intradermally injecting 0.1 mL of purified protein derivative tuberculin solution into the volar or dorsal surface of the forearm. This method is the recommended method for tuberculin skin testing.

mask: A device worn over the nose and mouth (e.g., surgical mask [not N95]) of a person with suspected or confirmed infectious TB disease to prevent infectious particles from being released into room air.

medical evaluation: An examination to diagnose TB disease or latent TB infection, to select treatment, and to assess response to therapy. A medical evaluation can include medical history and TB symptom screen, clinical or physical examination, screening and diagnostic tests (e.g., tuberculin skin tests, chest radiographs, bacteriologic examination, and human immunodeficiency virus testing), counseling, and treatment referrals.

meningeal TB: A highly dangerous and difficult-to-diagnose form of TB disease with infectious invasion of the tissues covering the brain. Often indolent but uniformly fatal if untreated, at times it is diagnosed too late to save the patient's life or prevent permanent disability.

miliary TB: A dangerous, and difficult to diagnose, form of rapidly progressing TB disease that extends throughout the body. Uniformly fatal if untreated, sometimes it is diagnosed too late to save the patient's life. Derives its name from a pathognomonic chest radiograph, but certain patients with this condition have normal findings or ordinary infiltrates on the chest radiograph. Sometimes referred to as disseminated TB.

multidrug-resistant TB (MDR TB): TB disease caused by an *M. tuberculosis* strain that is resistant to at least isoniazid and rifampin. Treatment regimens for curing MDR-TB are long, expensive, and difficult to tolerate. The cure rate depends on the susceptibility of *M. tuberculosis* to alternative second line drug therapy.

mycobacteria other than tuberculosis (MOTT): See **nontuberculous mycobacteria**.

Mycobacterium tuberculosis: The namesake member organism of *M. tuberculosis* complex and the most common causative infectious agent of TB disease in humans. In certain instances, the species name refers to the entire *M. tuberculosis* complex, which includes *M. bovis* and *M. african, M. microti, M. canetii, M. caprae,* and *M. pinnipedii*.

N95 disposable respirator: An air-purifying, filtering-face piece respirator that is more than 95% efficient at removing 0.3 μm particles and is not resistant to oil. See also **respirator**.

negative pressure: The difference in air-pressure between two areas. A room that is under negative pressure has a lower pressure than adjacent areas, which keeps air from flowing out of the room and into adjacent rooms or areas. Also used to describe a

nonpowered respirator. See also **airborne infection isolation** and **airborne infection isolation room**.

night sweats: Present in approximately 50% of cases of active TB patients complain of drenching diaphoresis that wakes them up at night.

nontuberculous mycobacteria (NTM): Refers to mycobacterium species other than those included as part of *M. tuberculosis* complex. Although valid from a laboratory perspective, the term can be misleading because certain types of NTM cause disease with pathologic and clinical manifestations similar to TB disease. Another term for NTM is mycobacterium other than tuberculosis. NTM are environmental mycobacteria.

nucleic acid amplification test (NAAT): A laboratory method used to target and amplify a single deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) sequence for detecting and identifying (typically) a microorganism. NAATs for *M. tuberculosis* complex are sensitive and specific; they can accelerate confirmation of pulmonary TB disease. NAAT can be used as a diagnostic test for TB, for more information see "Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis," at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm?s_cid=mm5801a3_e.

outbreak (TB): Relative to the local context. Outbreak cases can be distinguished from other cases only when certain associations in time, location, patient characteristics, or *M. tuberculosis* attributes (e.g., drug resistance or genotype) become apparent. In low-incidence jurisdictions, any temporal cluster is suspicious for an outbreak. A working definition of a potential "TB outbreak" is helpful for planning and response and may include any of the following 6 criteria:

Criteria based on surveillance and epidemiology:

- An increase has occurred above the expected number of TB cases.
- During and because of a contact investigation, 2 or more contacts are identified as having TB disease, regardless of their assigned priority, (i.e., high-, medium-, or low-priority).
- Any 2 or more cases occurring within 1 year of each other are discovered to be linked, and the linkage is established outside of a contact investigation (e.g., 2 patients who received a diagnosis of TB disease outside of a contact investigation are found to work in the same office and only 1 or neither of the persons was listed as a contact to the other).
- A genotype cluster leads to discovery of 1 or more verified transmission links which were missed during a contact investigation within the prior 2 years.

Criteria based on program resources:

- Transmission is continuing despite adequate control efforts by the TB control program.

- Contact investigation associated with increased cases requires additional outside help.

Perihilar: The area just above the lungs, surrounding the mediastinum. Lymph nodes can become enlarged in this area, which is often indicative of active TB in a child

periodic fit testing: Repetition of fit testing performed in accordance with federal, state, and local regulations. Additional fit testing should be used when 1) a new model of respirator is used, 2) a physical characteristic of the user changes, or 3) when the user or respiratory program administrator is uncertain that the healthcare worker is obtaining an adequate fit.

potential ongoing transmission: A risk classification for TB screening, including testing for *M. tuberculosis* infection when evidence of ongoing transmission of *M. tuberculosis* is apparent in the setting. Testing might need to be performed every 8–10 weeks until lapses in infection controls have been corrected and no further evidence of ongoing transmission is apparent. Use potential ongoing transmission as a temporary risk classification only. After corrective steps are taken, reclassify the setting as medium risk. Maintaining the classification of medium risk for at least 1 year is recommended.

Pott's disease: TB of the spine.

powered air-purifying respirator (PAPR): A respirator equipped with a tight-fitting face piece (rubber face piece) or loose-fitting face piece (hood or helmet), breathing tube, air-purifying filter, cartridge or canister, and a fan. Air is drawn through the air-purifying element and pushed through the breathing tube and into the face piece, hood, or helmet by the fan. Loose-fitting PAPRs (e.g., hoods or helmets) might be useful for persons with facial hair because they do not require a tight seal with the face.

prevalence: The proportion of persons in a population who have a disease at a specific time.

priority of contacts: A system for ranking contacts for investigation based upon the characteristics of the index patient, the duration and circumstances of the exposure, and the vulnerability/susceptibility of the contacts to disease from Mycobacteria infection. Dividing contacts into three levels provides a system for public health to reach high-priority contacts first, then medium- and low-priority contacts.

pulmonary TB: TB disease that occurs in the lung parenchyma, usually producing a cough that lasts 2 to 3 weeks.

purified protein derivative (PPD) tuberculin: A material used in diagnostic tests for *M. tuberculosis* infection. In the United States, PPD solution (5 tuberculin units per 0.1 mL) is approved for administration as an intradermal injection as a diagnostic aid for *M. tuberculosis* infection (latent infection or TB disease).

QuantiFERON®-TB Gold in-tube (QFT-GIT) and QuantiFERON®-TB Gold test (QFT-G): Interferon gamma release assays (IGRAs) that test for *M. tuberculosis* in blood. These tests for *M. tuberculosis* detect cell-mediated immune response to *M. tuberculosis* in heparinized whole blood from venipuncture. This test requires only a single patient encounter, and the result can be ready within 1 day. These tests appear to be capable of distinguishing between the sensitization caused by *M. tuberculosis* infection and that caused by bacille Calmette-Guérin vaccination. CDC released new Interferon Gamma Release Assays (IGRA) guidelines on June 25, 2010, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" *(MMWR* 2010; 59 [No. RR-5];1-25) at http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf.

radiography: The diagnostic imaging techniques (including plain-film chest radiographs and computerized tomography) that rely on degrees of X-radiation transmission related to differences in tissue densities.

reinfection: A second infection that follows from a previous infection by the same causative agent. Frequently used when referring to an episode of TB disease resulting from a subsequent infection with *M. tuberculosis* and a different genotype.

resistance: The ability of certain strains of mycobacteria, including *M. tuberculosis*, to grow and multiply in the presence of certain drugs that ordinarily kill or suppress them. Such strains are referred to as drug-resistant strains and cause drug-resistant TB disease. See also **multidrug-resistant TB**.

respirator: A Centers for Disease Control and Prevention (CDC)/National Institute for Occupational Safety and Health (NIOSH)-approved device (e.g., N95) worn to prevent inhalation of airborne contaminants.

respiratory hygiene and cough etiquette: Procedures by which patients with suspected or confirmed infectious TB disease can minimize the spread of infectious droplet nuclei by decreasing the number of infectious particles that are released into the environment. Patients with a cough should be instructed to turn their heads away from persons and to cover their mouth and nose with their hands or preferably a cloth or tissue when coughing or sneezing.

respiratory protection: The third level in the hierarchy of TB infection control measures (after administrative and environmental controls) is the use of respiratory protective equipment in situations in which the administrative and environmental controls do not eliminate the risk that exposures can still occur (e.g., airborne infection isolation rooms and rooms where cough-inducing or aerosol-generating procedures are performed).

risk assessment (TB): An initial and ongoing evaluation of the risk for transmission of *M. tuberculosis* in a particular healthcare setting. To perform a risk assessment, the

following factors should be considered: the community rate of TB, number of TB patients encountered in the setting, and the speed with which patients with TB disease are suspected, isolated, and evaluated. The TB risk assessment determines the types of administrative and environmental controls and respiratory protection needed for a setting.

screening (TB): An administrative control measure in which evaluation for latent TB infection and TB disease are performed through initial and serial screening of healthcare workers and homeless shelters, as indicated. Evaluation might comprise tuberculin skin test, blood assay for *M. tuberculosis*, chest radiograph, and symptom screening. See also **symptom screen**.

secondary (TB) case: A new case of TB disease that is attributed to recent transmission as part of the scenario under investigation.

sensitivity: See **drug susceptibility test**.

smear: A laboratory technique for preparing a specimen so bacteria can be visualized microscopically. Material from the specimen is spread onto a glass slide (and typically dried and stained). Smear, stain, and microscopy methods for mycobacteria are specific to this genus. The slide can be scanned by light or fluorescent high-power microscopy. These methods require ongoing quality assurance for prompt and reliable results. The results for sputum acid-fast bacilli (AFB) smears typically are reported as numbers of AFB per high-powered microscopy field, or else as a graded result, from no AFB to 4+ AFB. The quantity of stained organisms is associated with degree of infectiousness. See **acid-fast bacilli**.

source: The person or case that was the original source of infection for secondary cases or contacts. The source case can be, but is not necessarily, the index case.

source case investigation: An investigation to determine the source case could be conducted in at least 2 circumstances: 1) when a healthcare setting detects an unexplained cluster of tuberculin skin test conversions among healthcare workers or 2) when TB infection or disease is diagnosed in a young child. The purposes of a source case investigation are to ascertain that the source case has been diagnosed and treated, to prevent further *M. tuberculosis* transmission, and to ensure that other contacts of that source case are also evaluated and, if indicated, provided treatment.

specimen: Any bodily fluid, secretion, or tissue sent to a laboratory for testing.

sputum: Mucus-containing secretions coughed up from inside the lungs. Tests of sputum (e.g., smear and culture) can confirm pulmonary TB disease. Sputum is different from saliva or nasal secretions, which are unsatisfactory specimens for detecting TB disease.

sputum induction: A method used to obtain sputum from a patient who is unable to cough up a specimen spontaneously. The patient inhales a saline mist, which stimulates coughing from deep inside the lungs.

susceptibility: See **drug susceptibility test**.

suspected TB: A tentative diagnosis of TB that will be confirmed or excluded by subsequent testing. Cases should not remain in this category for longer than 3 months.

symptom screen: A clinical evaluation procedure in which patients are asked if they have experienced any departure from normal in function, appearance, or sensation related to TB disease (e.g., cough, weight loss, night sweats).

symptomatic: A term applied to a patient with health-related complaints (i.e., symptoms) that might indicate the presence of disease. In certain instances, the term is applied to a medical condition (e.g., symptomatic pulmonary TB).

targeted testing: A strategy to focus testing for infection with *M. tuberculosis* in persons at high risk for latent TB infection and for those at high risk for progression to TB disease if infected.

transmission: Any mode or mechanism by which an infectious agent is spread from a source through the environment or to a person (or other living organism). In the context of healthcare-associated TB infection control, transmission is the airborne conveyance of aerosolized *M. tuberculosis* contained in droplet nuclei from a person with TB disease, usually from the respiratory tract, to another person, resulting in infection.

transmission site: A place where exposure may have occurred and where *M. tuberculosis* may have been spread. Examples of transmission sites include homes, workplaces, correctional facilities, daycare settings, schools, and homeless shelters. Transmission sites have been identified also at other places where people regularly spend time together such as churches or bars. In addition, social networking analysis has found transmission sites at a group of locations where the same people meet regularly for activities such as floating card games.

treatment of contacts: A course of anti-TB medications determined by the evaluation of the contact. A contact at high risk of developing TB disease may undergo window prophylaxis for latent TB infection (LTBI) during the time period between the first and second tests for TB infection. If a contact is determined to have LTBI and not to have TB disease, the contact may undergo a full course of treatment (one drug) for LTBI (9 months) to prevent the progression of infection into TB disease. If the contact is determined to have TB disease, the contact is a secondary case and treated (four drugs) for TB disease (minimum of 6 months).

T-SPOT®.*TB* (T-Spot): An interferon gamma release assay (IGRA) that tests for *M. tuberculosis* in blood. T-Spot tests for *M. tuberculosis* by detecting cell-mediated immune response to *M. tuberculosis* in heparinized whole blood from venipuncture. This test requires only a single patient encounter, and the result can be ready within 1 day. These tests appear to be capable of distinguishing between the sensitization caused by *M. tuberculosis* infection and that caused by bacille Calmette-Guérin vaccination.

tubercle bacilli: *M. tuberculosis* organisms.

tuberculin: A precipitate made from a sterile filtrate of *M. tuberculosis* culture medium.

tuberculin skin test (TST): A diagnostic aid for finding *M. tuberculosis* infection. A small dose of tuberculin is injected intradermally (in the United States by the Mantoux method), and the area is examined for induration by palpation 48–72 hours after the injection. The indurated margins should be read transverse (perpendicular) to the long axis of the forearm. See also **Mantoux method** and **purified protein derivative (PPD) tuberculin**.

tuberculosis (TB) disease: Condition caused by infection with a member of the *M. tuberculosis* complex that has progressed to causing clinical illness (manifesting symptoms or signs) or subclinical illness (early stage of disease in which signs or symptoms are not present, but other indications of disease activity are present). The bacteria can attack any part of the body, but disease is most commonly found in the lungs (pulmonary TB). Pulmonary TB disease can be infectious, whereas extrapulmonary disease (occurring at a body site outside the lungs) is not infectious, except in rare circumstances. When the only clinical finding is specific chest radiographic abnormalities, the condition is termed “inactive TB” and can be differentiated from active TB disease, which is accompanied by symptoms or other indications of disease activity (e.g., the ability to culture reproducing TB organisms from respiratory secretions or specific chest radiographic finding). See also **infection**.

tuberculosis (TB) infection: See **infection**.

tuberculosis (TB) morbidity and mortality: Reported incidence of and death rates from TB.

two-step (tuberculin) skin test: A procedure used for baseline skin testing of persons who will periodically receive tuberculin skin tests (TSTs) (e.g., healthcare workers or residents of long-term–care facilities). Two-step TSTs are used to reduce the likelihood of mistaking a boosted reaction for a new infection. If an initial TST result is classified as negative, a second test is repeated 1 to 3 weeks later. If the reaction to the second TST is positive, it should be interpreted as evidence of infection with *M. tuberculosis* and indicates that the infection was most likely in the past and not recent. If the second TST is also negative, the person is classified as not being infected. Two-step skin testing has no place in

contact investigations or in other circumstances in which ongoing transmission of *M. tuberculosis* is suspected.

ultraviolet germicidal radiation (UVGI): An air-cleaning technology that can be used in a room or corridor to irradiate the air in the upper portion of the room (upper-air irradiation) and is installed in a duct to irradiate air passing through the duct (duct irradiation) or incorporated into room air-recirculation units. UVGI uses ultraviolet germicidal irradiation to kill or inactivate microorganisms.

wheal: A small bump that is produced when a tuberculin skin test (TST) is administered. The wheal disappears in approximately 10 minutes after TST placement.

window period: The interval between infection and detectable skin test reactivity is referred to as the window period and is estimated to be 2–12 weeks.

extensively drug-resistant tuberculosis (XDR-TB): The occurrence of TB in persons whose *M. tuberculosis* isolates are resistant to isoniazid and rifampin and also resistant to any fluoroquinolone and to at least 1 of 3 injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin).