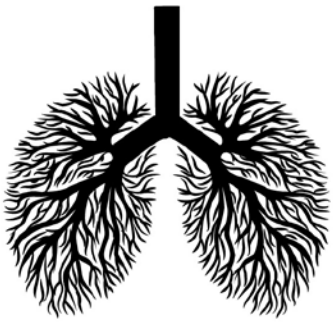
Alaska
Tuberculosis
Program Manual



Alaska Department of Health and Social Services

Table of Contents

INTRODUCTION

SURVEILLANCE

TARGETED TESTING FOR LATENT TUBERCULOSIS INFECTION

B NOTIFICATIONS

DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION

TREATMENT OF LATENT TUBERCULOSIS INFECTION

DIAGNOSIS AND TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI) AND TUBERCULOSIS DISEASE IN CHILDREN (UNDER 16 YEARS OF AGE)

CASE MANAGEMENT

CONTACT INVESTIGATION

LABORATORY SERVICES

PATIENT EDUCATION

Introduction

CONTENTS

About the Alaska Tuberculosis Program Manual

Purpose

This manual is designed to present the key steps and crucial information needed to perform tuberculosis (TB) prevention and control tasks in Alaska.[1] Where additional or more detailed information is available, hyperlinks to CDC guidelines and other resources are provided.

Audience

The audience for this manual includes physicians, physicians assistants, nurses, nurse practitioners, public health nurses; infection control nurses, and community health aides/practitioners.

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 **18.1**.

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.

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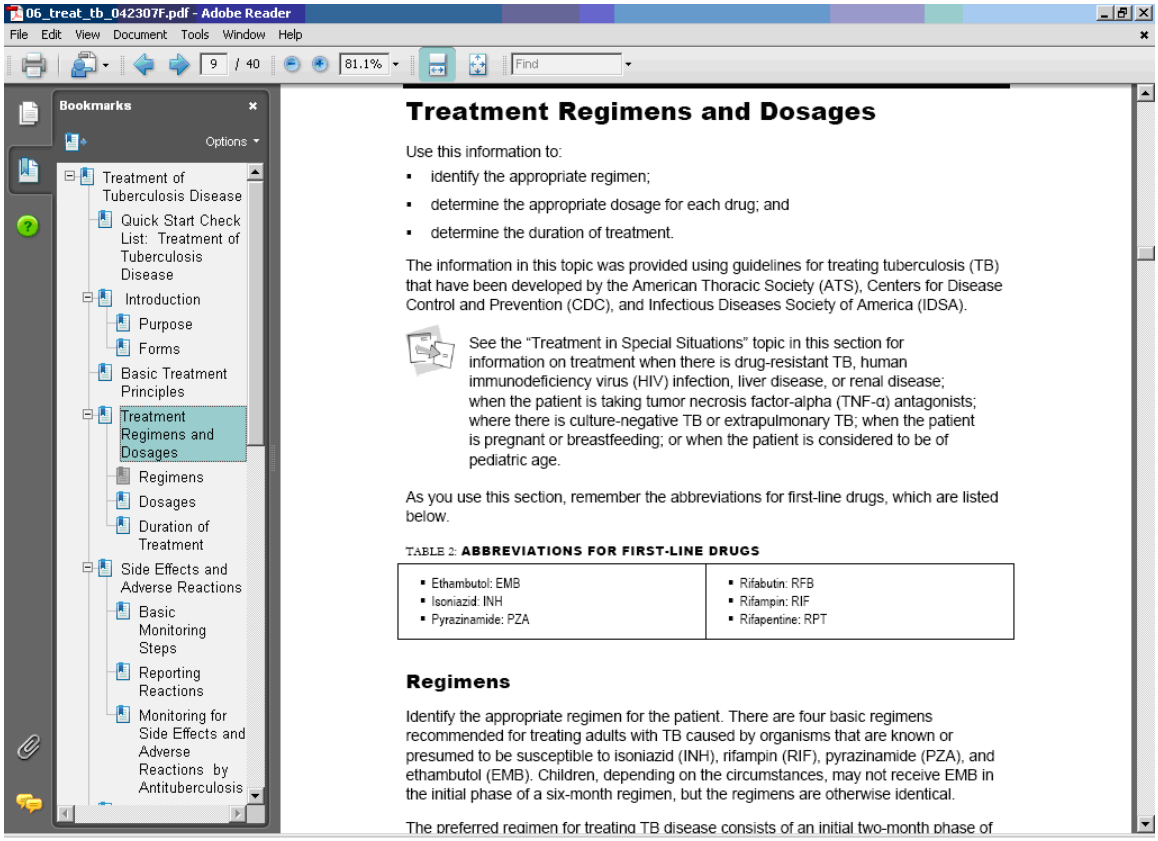

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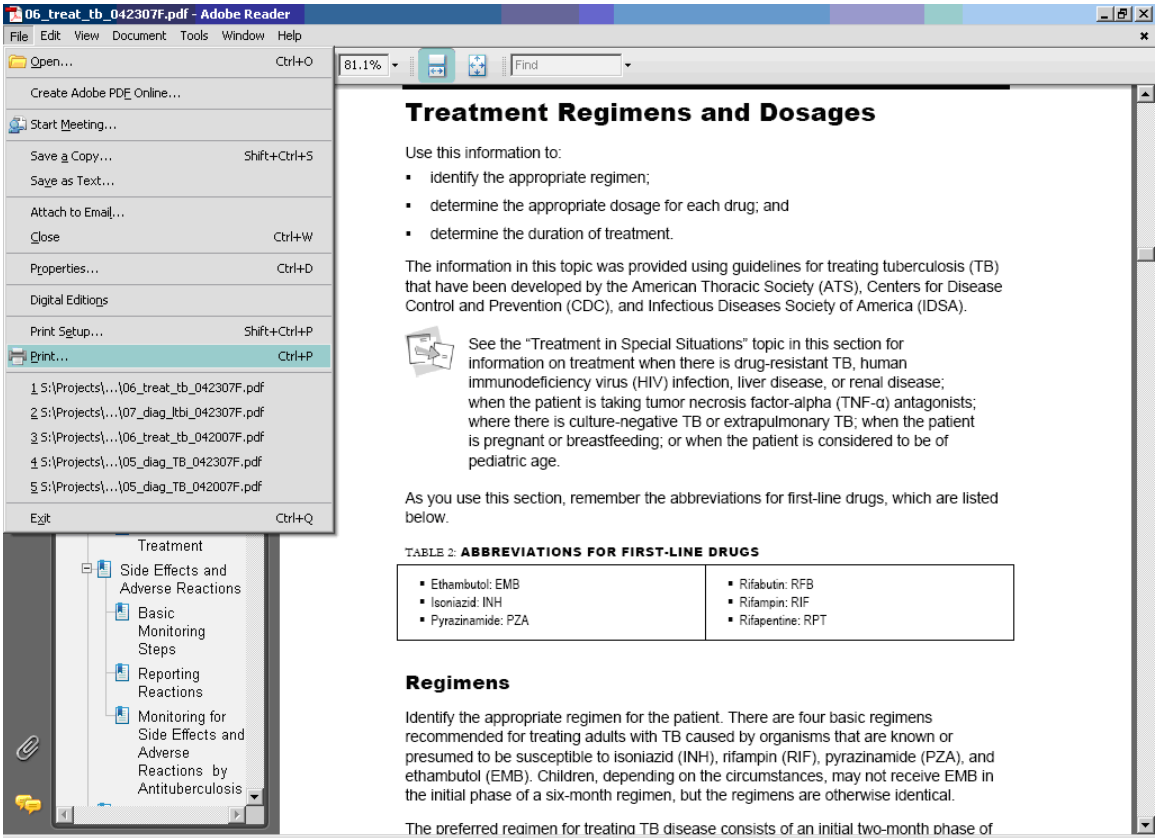

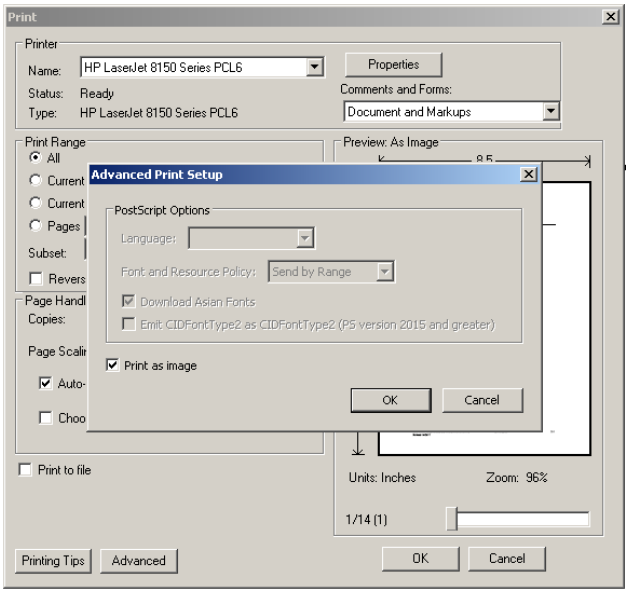

Some printers have older printer drivers that cause spaces to appear in the middle of words. To avoid this problem, click File/Print, click the Advanced button, check Print as Image, and then click OK.

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
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
NTM	nontuberculous mycobacteria
NTNC	National Tuberculosis Nurse Coalition
OSHA	Occupational Safety and Health Administration
PAPR	powered air-purifying respirator
PCR	polymerase chain reaction
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
TB	tuberculosis
TIMS	Tuberculosis Information Management System
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. These mycobacteria are *M. tuberculosis, M. bovis,* and *M. africanum.* 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

- 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 contracted *M. tuberculosis* infection.[2]

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) online course *Interactive Core Curriculum on Tuberculosis* (2013) at http://www.cdc.gov/tb/education/ce/interactive-corecurr.htm .

The four fundamental strategies to reduce TB morbidity and mortality are

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; and
4. identification of settings in which a high risk exists for transmission of *M. tuberculosis* and application of effective infection control measures.[3]

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 .

Alaska Statutes and Regulations on Tuberculosis Control

Alaska Statutes and Regulations pertaining to the control of tuberculosis in Alaska are available in the Statutes and Regulations section of the manual **19.1**.

Objectives and Standards

Quality of Care

For tuberculosis (TB) programs, quality of care is measured by means of objectives. Such objectives are used as yardsticks to direct the program and measure its success.

Objectives reflect outcomes or results and program desires. Programs require objectives to define expected outcomes and results for case management activities.

In Alaska, TB program objectives are established from the following:

State Statutes and Regulations

Alaska Statutes and Regulations pertaining to the control of tuberculosis in Alaska are available in the Statutes and Regulations section of the manual **19.1**.

This information can also be found online in "Conditions Reportable to Public Health"
at http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.aspx

TB Program Agreements, Plans, and Protocols

Centers for Disease Control and Prevention (CDC) Cooperative Agreement

A copy of Alaska's current "Tuberculosis in Alaska Annual Report" is available at the Tuberculosis Program website
http://dhss.alaska.gov/dph/Epi/id/Pages/tb.aspx

National and State Program Objectives

Below are national and select state TB program objectives. The CDC program objectives are current as of August 2015.[4] Under targeted national objectives, there are state objectives established by the Alaska TB Program, based on Alaska's epidemiology and recent program performance.

Table 1: NATIONAL TUBERCULOSIS PROGRAM OBJECTIVES AND PERFORMANCE TARGETS FOR 2020

Goals for Reducing TB Incidence		Targets
TB Incidence Rate	Reduce the incidence of TB disease.	1.4 cases per 100,000
U.S.-Born Persons	Decrease the incidence of TB disease among U.S.-born persons.	0.4 cases per 100,000
Alaska Objective	*Decrease the incidence of TB disease among U.S.-born persons who are not Alaska Native*	*0.4 cases per 100,000*
Foreign-Born Persons	Decrease the incidence of TB disease among foreign-born persons.	11.1 cases per 100,000
U.S.-Born Non-Hispanic Blacks or African Americans	Decrease the incidence of TB disease among U.S.-born non-Hispanic blacks or African Americans.	1.5 cases per 100,000
Alaska Objective	*Decrease the incidence of TB disease among Alaska Native persons.*	*20 cases per 100,000*
Children Younger than 5 Years of Age	Decrease the incidence of TB disease among children younger than 5 years of age.	0.3 cases per 100,000
Objectives on Case Management and Treatment		**Targets**
Known HIV Status	Increase the proportion of TB patients who have a positive or negative HIV test result reported.	98%
Treatment Initiation	For TB patients with positive acid-fast bacillus (AFB) sputum-smear results, increase the proportion who initiated treatment within 7 days of specimen collection.	97%
Recommended Initial Therapy	For patients whose diagnosis is likely to be TB disease, increase the proportion who are started on the recommended initial 4-drug regimen.	97%
Sputum Culture Result Reported	For TB patients ages 12 years or older with a pleural or respiratory site of disease, increase the proportion who have a sputum culture result reported.	98%
Sputum Culture Conversion	For TB patients with positive sputum culture results, increase the proportion who have documented conversion to negative results within 60 days of treatment initiation.	73%
Completion of Treatment	For patients with newly diagnosed TB disease for whom 12 months or less of treatment is indicated, increase the proportion who complete treatment within 12 months.	95%

Adapted from Source: CDC. National TB Program Objectives & Performance Targets for 2020. Available at: https://www.cdc.gov/tb/programs/evaluation/pdf/programobjectives.pdf

National Standards, Guidelines and 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 ATS, IDSA and CDC, and generally recognized TB control experts, such as the National Tuberculosis Nurse Coalition (NTNC) and National Tuberculosis Controllers Association (NTCA).

The standards of care for the medical treatment and control of TB are published jointly by the American Thoracic Society (ATS), the Infectious Diseases Society of America (IDSA), and the 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. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/cid_ciw694_full.pdf .
- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .
- A. "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 27, 2016). Available at: http://www.cdc.gov/tb/publications/guidelines/default.htm .

Roles, Responsibilities, and Contact Information

State TB Program Staff

Table 2: ALASKA TUBERCULOSIS CONTROL PROGRAM STAFF ROLES, RESPONSIBILITIES, AND CONTACT INFORMATION

Roles and Responsibilities	Contact Information
Alaska TB Controller / Medical Epidemiologist Establishes short and long range program goals for prevention of infection and controlling disease; directs the planning, implementation and evaluation of program activities/special projects, develops program policies, procedures and standards; writes TB grant applications; provides oversight of preparation, allocation and monitoring of program resources and budget; conducts infectious disease surveillance and analyzes tuberculosis data; supervises the maintenance of appropriate records and data collection systems; and responds to inquiries regarding interpreting state TB laws and regulations. Provides medical consultation and education to healthcare providers statewide who diagnose and treat patients with TB or LTBI. Also provides consultation to PHNs in areas of TB case management, including DOT. Provides medical evaluation of chest radiograph and patient history and makes recommendations for LTBI therapy. Responds to inquiries from the general public, media and legislators regarding TB morbidity, disease outbreaks and disease trends. Provides consultation and technical assistance to local health agencies, schools, clinics, long-term care facilities, correctional facilities, homeless shelters, and other public and private agencies regarding TB policies and procedures. Determines need for legal actions such as quarantine and isolation.	Vacant Section of Epidemiology 3601 C Street, Suite 540 Anchorage, AK 99503 Tel: 907-269-8000 Fax: 907-563-7868 E-mail:

Roles and Responsibilities	Contact Information
Alaska TB Program Nurse Consultant Provide statewide consultations to public health nurses (PHNs), physicians, other health care providers, hospitals, schools, long-term care facilities, homeless shelters, correctional systems and other agencies regarding TB program standards of care for case management, contact investigation, treatment of LTBI, and directly observed therapy. In partnership with the Section of Public Health Nursing (SOPHN), coordinate TB case management and participate in case management teleconferences with local PHNs. Conduct tuberculosis outbreak investigations and assist with large contact investigations. Conduct training for health care providers statewide. Provide phone consultations to the general public.	Donna Fearey, RN, ANP, MSN Section of Epidemiology 3601 C Street, Suite 540 Anchorage, AK 99503 Tel: 907-269-8000 Fax: 907-562-7802 E-mail: donna.fearey@alaska.gov

Roles and Responsibilities	Contact Information
Alaska Public Health Nurses and Grantees Alaska Public Health Nurses (PHNs) play a vital role in the prevention and control of tuberculosis. **Case Management** Conduct local case management for all cases of active TB, order TB medications from the state pharmacy, set up and monitor directly observed therapy (DOT) at the community level for all infectious cases, participate in case management teleconferences with the Alaska TB Program, work with primary care provider on TB standards of care as needed. Conduct patient education as needed. **Contact Investigation** Lead contact investigations and adequately test contacts, identify contacts needing therapy for latent TB infection (LTBI), order meds through state pharmacy, monitor LTBI therapy, including establishing DOT for high-risk persons with LTBI. Document and report all contact investigation activities and follow-up to the Alaska TB Program. **TB Prevention and Screening** Facilitate targeted testing of high-risk populations on a case-by-case basis.	Linda K. Worman, D.M., RN Chief, Section of Public Health Nursing P.O. Box 110611 Juneau, AK 98111-0611 Tel: 907-465-3150 Fax: 907-465-3913 E-mail: linda.worman@alaska.gov Information about public health centers across the state is available at: http://dhss.alaska.gov/dph/Nursing/Pages/locations.aspx

Immigrant and Refugee Screening Conduct TB screening for immigrants and refugees and provide LTBI therapy as needed. Document and report all screening activities and follow-up to the Alaska TB Program.	

Local Public Health Agencies

Table 3: LOCAL PUBLIC HEALTH AGENCIES' ROLES, RESPONSIBILITIES, AND DIRECTORY

Roles and Responsibilities	Contact Information
The Municipality of Anchorage Health and Human Services, Community Health Services, Disease Prevention and Control Provides tuberculosis screening, case management for persons with suspect or active TB, contact investigation, and immigrant and refugee screening.	TB Control Program 825 L Street, 1st Floor Anchorage, AK 99503 Tel: 907-343-4799 Fax: 907-343-7992 Information about TB services provided by the Municipality of Anchorage is available at: http://www.muni.org/Departments/health/community/Pages/Disease.aspx

Private Medical Providers

Table 4: PRIVATE MEDICAL PROVIDERS ROLES AND RESPONSIBILITIES

Role and Responsibilities
1. Report all suspected or confirmed cases of tuberculosis to the Section of Epidemiology within 5 working days of evaluation.
2. Conduct initial patient evaluation and periodic follow-up with the patient.
3. Prescribe tuberculosis medications and send prescription to local public health nurse. Medications will be supplied free-of-charge from the state pharmacy.
4. Provide adequate and understandable instruction in disease control measures to each patient who has been diagnosed with active tuberculosis.
5. Maintain responsibility for deciding date of discharge for hospitalized tuberculosis patients and consult with the Alaska TB Program regarding plans for public health follow-up of the patient in the community.

Laboratories

TABLE 5: LABORATORIES' ROLES, RESPONSIBILITIES AND DIRECTORY

Role and Responsibilities	Contact Information
State Laboratory The Alaska State Public Health Laboratory (ASPHL) is an integral part of the Division of Public Health and the Alaska Tuberculosis l Program. As the state's only reference laboratory, the ASPHL provides clinics, hospitals and other health care agencies, a wide range of services including identification and confirmation of pathogenic organisms. In addition, it provides susceptibility testing for all isolates of *M. Tuberculosis* (MTB) and sends all isolates to the national genotyping project. The TB Unit receives and processes MTB specimens five days a week. Microscopic results are provided within 24 hours of receipt except on weekends and holidays. The Acid-Fast Bacilli (AFB) positive results received by the ASPHL are entered into a lab database and reported within a day (by phone or fax) to submitting laboratories, health care providers and the Alaska TB Program. Using state of the art technology, the unit performs isolation and definitive identification on all mycobaterial isolates received by ASPHL. 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 first line drugs.	Alaska State Public Health Laboratory Bernd Jilly, PhD 5455 Dr. Martin Luther King Jr. Ave. PO Box 196093 Anchorage, AK 99507 Tel: (907) 334-2100 Fax: (907) 334-2161 E-mail: bernard.jilly@alaska.gov Additional information about state laboratory services is available at: http://www.hss.state.ak.us/dph/labs/
Private Laboratories There are a number of reference laboratories in communities across the state. It is recommended that specimens for *M. Tuberculosis* (MTB) testing be submitted to ASPHL.	

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 January 25, 2017). Available at: http://www.cdc.gov/tb/programs/Evaluation/Guide/PDF/Complete_guide_Developing_eval_plan.pdf .
- Division of Tuberculosis Elimination. *Understanding the TB Cohort Review Process: Instruction Guide* (Division of Tuberculosis Elimination Web site; accessed January 25, 2017). 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://globaltb.njms.rutgers.edu/downloads/planning&implementing/TBCaseMGT.pdf .

References

[1] CDC. Progressing toward tuberculosis elimination in low-incidence areas of the United States: recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 2005;51(No. RR-5):1.
[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):14.
[3] 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.
[4] CDC. National TB Program Objectives & Performance Targets for 2020. Available at: https://www.cdc.gov/tb/programs/evaluation/pdf/programobjectives.pdf

Surveillance

CONTENTS

Introduction

Purpose

Use this section to

- 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 computerized TB registry works; and
- 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

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; and
5. strategically plan 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 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 Section of Epidemiology 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. **2.9**

For a list of reportable diseases, including tuberculosis and instructions on how to report in Alaska, see *Conditions Reportable to Public Health at* http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.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.[5] 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., defining 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. **11.47**

Contact investigation: Collecting, analyzing, interpreting, and disseminating data on contacts and contact investigations are necessary for prioritizing the highest-risk contacts, resulting in focused 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.[6]

For more information on surveillance in contact investigations, see the Contact Investigation section. **11.1**

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, to prevent subsequent progression to TB disease. Targeted testing and treatment of LTBI is 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 the Targeted Testing section. **3.1**

Treatment of LTBI: Surveillance of persons with LTBI does not routinely occur in the United States. However, the CDC is developing a national surveillance system to record adverse events leading to the hospitalization or death of a person under treatment for LTBI. Healthcare providers are encouraged to report such events to the CDC's Division of Tuberculosis Elimination by calling 1-404-639-8401. 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 *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* available at: https://www.cdc.gov/tb/publications/ltbi/treatment.htm#treatmentRegimens

Policy

Data collection and reporting on TB should be done in accordance with Alaska statutes 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. **1.8**

For more information on confidentiality and the Health Insurance Portability and Accountability Act (HIPAA), see the Confidentiality section. **14.3**

State Statutes and Regulations

Several Alaska statutes and regulations govern infectious diseases, including tuberculosis, reporting and control. Suspected or confirmed cases of tuberculosis are reportable by law within five (5) working days.

See the Statutes and Regulations section of this manual **19.1** or *Conditions Reportable to Public Health, pages 5-46,* http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/ConditionsReportable.pdf .

Contact the Alaska TB Program at 907-269-8000 for assistance with interpreting state laws and regulations regarding TB control.

Reporting Tuberculosis

Detecting and reporting suspected cases of tuberculosis (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. 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.[6] 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.[7] By Alaska statute and regulation, a suspected or confirmed case of TB disease in Alaska must be reported to the Section of Epidemiology (907-269-8000) within five working days; however reports should be made as soon as possible.

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."[8] These criteria are listed below in Table 1.[9]

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.[10]

Confirmed: A case that meets the clinical case definition or is laboratory confirmed, as described below in Table 1.[11]

Table 1: CASE DEFINITIONS[12]

Clinical Case Definition	Laboratory Criteria for Diagnosis
A case that meets of the following criteria: ▪ A positive tuberculin skin test ▪ Other signs and symptoms compatible with tuberculosis (e.g., an abnormal, unstable [i.e., worsening or improving] chest radiographs, or clinical evidence of current disease) ▪ Treatment with two 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. NAA is not available in Alaska.

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 medical history, signs, symptoms, and radiographic findings of TB are evident among adults or children. TB should be suspected in any patient who has a persistent cough for over two to three weeks, or other indicative signs and symptoms.[13]

For more information on suspected pulmonary TB, see the Diagnosis of Tuberculosis Disease section. **5.10**

Mandatory and timely case reporting from community sources (e.g., providers, and laboratories) 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.[14]

Prompt reporting (prior to culture confirmation) allows the Alaska TB Program to do the following quickly:

- Verify the diagnosis
- Assign a public health nurse (PHN) Codirose5
- case manager and coordinate treatment
- Determine if an outbreak is occurring
- Control the spread of TB[15]

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.[16]

Reporting gives physicians access to resources provided by the local public health agency. Private physicians are encouraged to work collaboratively with their local public health agency in the management of their TB cases and contacts. All providers who undertake evaluation and treatment of patients with TB must recognize that, not only are they delivering care to an individual, they are assuming an important public health function that entails a high level of responsibility to the community, as well as to the individual patient.

The Alaska TB Control Program provides the following public health services to assist physicians and other health care providers with managing their TB cases:

- Epidemiologic investigation, including identification and examination of contacts
- Chest radiographic services
- Antituberculosis medications
- Case management by a PHN
- Public health laboratory laboratory services and consultation: All *M.tuberculosis* isolates should be sent to the Alaska State Public Health Laboratory (ASPHL) so that genotyping can be performed. [17]

For more information on confidentiality and the Health Insurance Portability and Accountability Act (HIPAA), see the Confidentiality section **14.3**

Reporting Suspected or Confirmed Cases of Tuberculosis to the Section of Epidemiology

Healthcare providers and laboratories should report suspected or confirmed cases of TB using the information in Table 2.

Table 2: WHEN TO REPORT TUBERCULOSIS

What Condition/ Test Result	Who Reports	When to Report	How to Report
Suspected or confirmed cases of tuberculosis (TB) disease Confirmation by laboratory tests is not required. This includes pulmonary and extrapulmonary cases.	Health care providers Note: The attending physician or other healthcare provider must report even if the laboratory is also reporting the test results.	Reports should be made as soon as possible and must be made within five working days	Alaska TB Program Staff 1-907-269-8000 during work hours 1-800-478-0084 after hours Fax 1-907-561-4239
Sputum smears positive for acid-fast bacilli (AFB) Nucleic Amplification (NAA) tests; polymerase chain reaction (PCR) or GeneXpert positive for *M. tuberculosis* complex Cultures that are positive for *Mycobacterium tuberculosis* complex* DNA probes positive for *M. tuberculosis* complex	All laboratories that perform TB testing In-state laboratories that send specimens for out-of-state testing Note: The laboratory must report even if the attending physician or other healthcare provider is also reporting.	Reports should be made as soon as possible and must be made within five working days	Alaska TB Program Staff 1-907-269-8000 during work hours 1-800-478-0084 after hours Rapid Telephonic Reporting Statewide 1-800-478-1800 Anchorage 1-907-561-4234 Fax 1-907-561-4239
* Note: Preliminary report of cultures growing AFB without confirmation of *M. tuberculosis* complex; final report of cultures that are demonstrated to be positive for *M. tuberculosis* complex.			

Use the *Infectious Disease Report Form* to report suspected and confirmed cases of TB. It is available at:

http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/frmInfect.pdf

Tuberculosis Case Information to Report to the Alaska TB Program

Healthcare Providers

Healthcare providers attending patients with confirmed or suspected TB should provide the following information to the Alaska TB Program, if available.

Patient Information

- Name
- Address
- Phone numbers
- Marital status
- Occupation
- Hospital admission information (name, admission date, etc.)
- Type of isolation arrangements (if applicable, home, hospital, other)
- Date of anticipated discharge and tentative discharge plan

Demographic and Social Information

- Date of birth
- Sex
- Race/ethnic origin
- Country of birth/date of U.S. arrival
- Drug and alcohol use
- Homeless within past year?
- Diagnosed in a correctional facility or long-term care facility?

Medical Information

- Reason for test
- Symptoms/onset
- Disease site
- Co-morbid health conditions
- Human immunodeficiency virus (HIV) testing information
- Results of QuantiFERON®-TB Gold (QFT-G) or tuberculin skin test (TST) (TST in mm) and date of test
- Chest radiograph results and dates (if applicable)
- Bacteriology results, date(s), and name of laboratory performing test(s)
- Drug therapy (medications used, dosages, start dates and dates given, mode of treatment)

Provider Information

- Names of primary and other physicians, discharge planners, case managers, social workers, etc.
- Phone numbers

Laboratories

Laboratories should report the following information on test results.

Reporting Laboratory

- Name
- Address
- Phone number
- Date of report

Sputum Smears Positive for Acid-Fast Bacilli (AFB)

- Collection date
- Specimen source
- Result

Cultures Growing AFB or Cultures Positive for *Mycobacterium tuberculosis*

- Collection date
- Specimen source
- Result

Nucleic acid amplification tests/DNA probes positive for *M. tuberculosis* complex

- Collection date
- Specimen source
- Result

Data Collection

Forms

The following standardized forms may be useful to document reporting activities and then placed in the patient's chart (Table 3). Additional forms pertaining to TB diagnosis, treatment and case management will be discussed in those sections.

Table 3: RECOMMENDED FORMS FOR A TUBERCULOSIS PATIENT'S CHART

Chart of a Patient on Treatment for Tuberculosis Disease	
Tuberculosis (TB) Disease Treatment/Case Management ▪ Infectious Disease Report Form ▪ TB Case Management Form ▪ Tuberculosis Treatment Contract Contact Investigation ▪ Contact Investigation Form	Transfer Notifications ▪ Interjurisdictional TB Notification ▪ Interjurisdictional TB Notification Follow-Up

To download the recommended forms go to the Forms section of the manual. **18.1**

Computerized Tuberculosis Registry

To carry out mandatory community public health responsibilities, the Alaska TB Program maintains a computerized record system (case registry) with information on all current clinically active and suspected TB cases.[18] Critical medical information is gathered on cases so that each case is optimally managed during their TB treatment.

The following information is maintained on each patient:[19]

- Acid-fast bacilli smear results
- Culture results
- NAA test results
- Drug susceptibility results

- Clinical status
- Chest radiograph results
- Drug regimen information
- Doses of medications being administered

Document Retention

The Alaska TB Program maintains all state TB public health records according to the Alaska Records Retention schedule.

Active TB case records are retained at the Alaska TB Program offices for at least seven years beyond completion of case follow-up; electronic case information is kept indefinitely. Paper records on individuals who were suspected to have tuberculosis are kept on-site for seven years after completion of follow-up. Electronic records on persons treated for latent tuberculosis infection or with suspected tuberculosis are available from 2000 forward are kept indefinitely.

Radiographs/ digital films are not stored by the state. Case management health information and other TB records should be maintained at the local public health agency according to current applicable record retention rules and regulations.

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).

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.

All *Mycobacterium tuberculosis* isolates in Alaska are submitted for genotyping. Suspected clusters are investigated to determine whether an outbreak has occurred.

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 positive *M. tuberculosis* cultures should be sent to the Alaska Public Health Laboratory in Anchorage for submission to the appropriate national genotyping laboratory.

Dissemination and Evaluation

Dissemination

Tuberculosis (TB) surveillance data are disseminated periodically to healthcare providers, health agencies, and the public through multiple channels including the Epidemiology Bulletin and annual report which can be found on the Alaska TB Program website. http://epibulletins.dhss.alaska.gov/Bulletin/DisplayClassificationBulletins/39

Evaluation

Alaska TB surveillance data are routinely evaluated to determine the status of TB in Alaska. The Alaska TB Program uses this information to develop public health actions that will help reduce the burden of TB in Alaska In addition the surveillance system is evaluated periodically to ensure that it operates to meet its purpose and objectives.

For more information see the CDC's "Updated Guidelines for Evaluating Public Health Surveillance Systems" (*MMWR* 2001;50[No RR-13]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5013a1.htm

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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):10.

[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):10.

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[4] 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.

[5] 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):39.

[6] 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):3.

[7] 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.

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

[9] CDC. *Reported Tuberculosis in the United States, 2004.* Atlanta, GA: US Department of Health and Human Services, CDC; September 2005. Appendix B, Section V.

[10] CDC. *Reported Tuberculosis in the United States, 2004.* Atlanta, GA: US Department of Health and Human Services, CDC; September 2005. Appendix B, Section V.

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

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

[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.

[14] ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

[15] County of Los Angeles Tuberculosis Control Program. *Tuberculosis Control Program Manual: 2003 Edition* [County of Los Angeles Public Health Web site]. 2003;8–6. Available at: http://www.lapublichealth.org/tb/TBManual/TBmanual.pdf . Accessed February 7, 2007.

[16] County of Los Angeles Tuberculosis Control Program. *Tuberculosis Control Program Manual: 2003 Edition* [County of Los Angeles Public Health Web site]. 2003;8–7. Available at: http://www.lapublichealth.org/tb/TBManual/TBmanual.pdf . Accessed February 7, 2007.

[17] ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

[18] CDC. Essential Components of a Tuberculosis Prevention and Control Program Screening for Tuberculosis and Tuberculosis Infection in High-Risk Populations: Recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1995;44(No. RR-11):14.

[19] CDC. Essential Components of a Tuberculosis Prevention and Control Program Screening for Tuberculosis and Tuberculosis Infection in High-Risk Populations: Recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1995;44(No. RR-11):14.

Targeted Testing for Latent Tuberculosis Infection

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska guidelines to conduct targeted testing to screen for latent tuberculosis infection (LTBI).

In the 2005 guideline "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of tuberculosis (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]

For information on treatment, refer to the Treatment of Tuberculosis Disease **(6.2)** and Treatment of Latent Tuberculosis Infection **(8.2)** sections.

Reducing LTBI in high-risk populations is an important strategy to control TB. With an estimated 9.5–14.7 million persons with LTBI in the United States, continued progress toward eliminating TB in the United States and reducing TB among foreign-born persons requires effective strategies to meet this challenge.[2] Targeted 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 *Mycobacterium tuberculosis* and those who have clinical conditions that are associated with an increased risk for progression of LTBI to active TB.[3]

Policy

In Alaska

- 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 and reported as suspected cases of TB as described in the "Reporting Tuberculosis" topic in the Surveillance section.
- Contacts should be evaluated as described in the Contact Investigation section.
- TB screening in schools and certain employment settings is required by regulation and described under "Program Standards" in this section.
- Targeted testing for LTBI should be conducted only among persons in groups with identified risk factors for LTBI and/or progression to TB disease.

- For a list of groups with increased likelihood of infection with Mtb, refer to Figure 1: Paradigm for evaluation of those with latent tuberculosis infection (LTBI) based on risk of infection, risk of progression to tuberculosis, and benefit of therapy**.**

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

State Laws and Regulations

See the Statutes and Regulations section for more information on:

7 AAC 27.213. Tuberculosis skin test
http://www.legis.state.ak.us/basis/aac.asp#7.27.213

7 AAC 12.571. Employee health program
http://www.legis.state.ak.us/basis/aac.asp#7.12.571

7 AAC 12.650. Employee health program
http://www.legis.state.ak.us/basis/aac.asp#7.12.650

Tuberculosis Assessment / Screening of School Children: Program Standards

The State of Alaska has moved away from universal tuberculosis (TB) screening for different ages of school children to risk-based assessment.

Alaska law requires that each public school district and nonpublic school offering pre-elementary education through the 12th grade, or a combination of these grades, shall assess the tuberculosis status of each child not later than 90 days after school enrollment. The department will inform each public school district and each nonpublic school about the appropriate tuberculosis screening strategy that the district or school shall employ. The strategy may consist of annual health surveys upon registration, PPD skin tests, alternative laboratory-approved methods for assessing tuberculosis status, or a combination of two or more of those approaches. The department will use one or more of the following criteria to determine the required screening strategy for a public school district or nonpublic school:

(1) evidence that prior PPD skin testing of school children in a community served by the district or school demonstrates tuberculosis transmission;

(2) evidence that tuberculosis disease is occurring in a community served by the district or school;

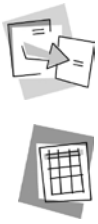
(3) evidence that a community served by the district or school has a history of high rates of tuberculosis when compared to rates of tuberculosis for the United States or this state;

(4) evidence that children from populations having a high risk of tuberculosis are enrolled in the district or school; in this paragraph, "populations having a high risk" includes groups that historically have been medically underserved, homeless persons, foreign-born persons from countries with high rates of tuberculosis, and persons with immune deficiency conditions. (27 AAC 27.213)

In Alaska, schools have been directed to screen students for TB by the Department of Health and Social Services, Division of Public Health per 7 AAC 27.213 according to TB activity or risk, including the presence of high risk populations. Schools in areas of **low TB risk**, such as Anchorage, Fairbanks, Juneau, Kenai, etc., as now designated as low risk schools and are required to do risk assessments for NEW SCHOOL ENTERERS ONLY and provide TSTs to those students with identified risk. Blood tests, called interferon gamma release assays (IGRA), may be used instead of TSTs to screen students who require TB testing. Currently, the Alaska TB Program and state public health nurses (PHNs) are unable to provide or pay for IGRA testing; it would be the parent or guardian responsibility to obtain, pay for, and provide the results of IGRA testing to the school to satisfy the regulatory testing requirement. Schools in areas of the state with **high TB risk** or activity, such as the Yukon Kuskokwim Delta, Norton Sound, etc., are now classified as high risk schools and are required to screen every student annually for TB by TSTs.

Superintendents are notified in writing regarding the risk category – high or low TB risk – assigned to their schools in addition to the required method(s) for TB screening and reporting in those schools. Tuberculosis screening of school children is done by PHN public health nurses at schools which lack personnel capable of conducting the testing. The school district is responsible for collecting the risk assessment and/or obtaining a consent form signed by the child's parent or guardian prior to administration of a tuberculin skin test to a child in the parent's absence. Prior BCG vaccination is not a contraindication to tuberculin skin testing.

It is also the school district's responsibility to suspend a child under AS 14.30.045 (4) if "…(1) the district or school has not screened the child for tuberculosis; or ; or (2) the child or a person acting on behalf of the child fails to provide the district or school, within 30 days after referral under (b) of this section [if a PPD skin test or other laboratory screening test is positive], a written and signed statement of a health care provider stating that the child is not infectious from tuberculosis to others." (27 AAC 27.213).



For detailed information on School TB assessment / screening and reporting, please see "School TB Screening Resources" on our website: http://dhss.alaska.gov/dph/Epi/id/Pages/tb.aspx

High-Risk Groups

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or for progression to TB disease. Testing for LTBI should be considered for persons with increased likelihood of infection with Mtb as listed in Figure 1. Providers making treatment decisions should assess not only the likelihood of infection and risk of progression to active TB if infected, but also the benefit of treatment.

Alaska Natives, particularly persons from the Southwest and Northern regions, have an increased likelihood of infection with Mtb due to the current and historic epidemiology of tuberculosis in our state.

Figure 1. PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY[4]

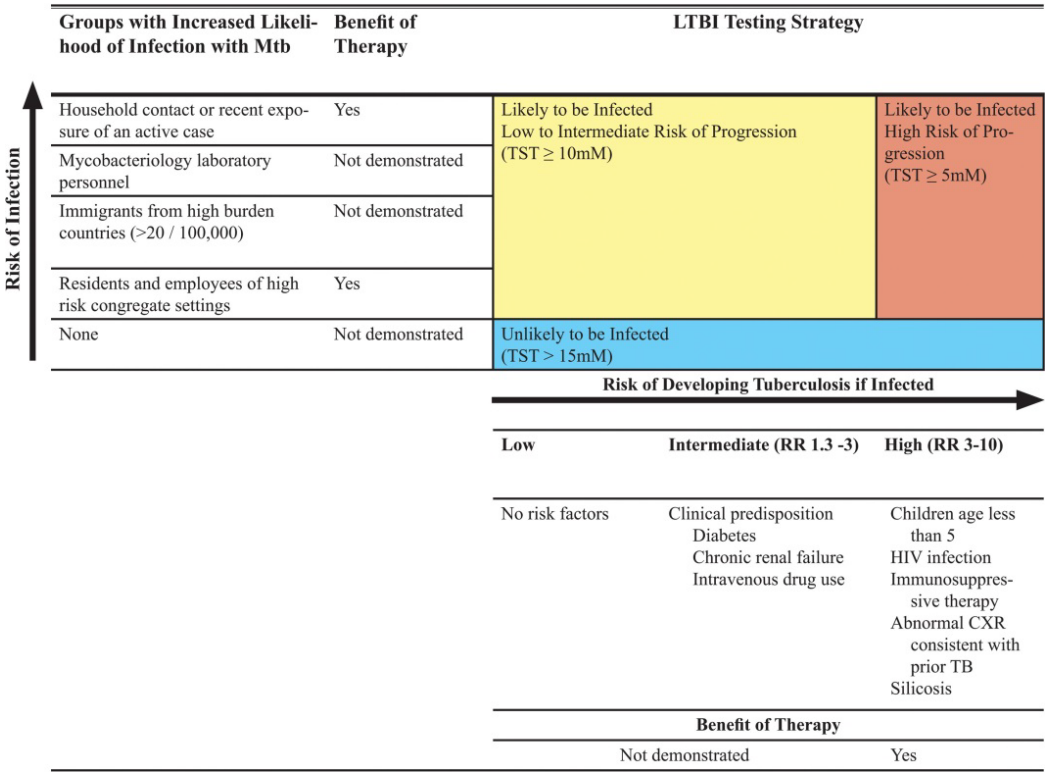


Figure 1. In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to tuberculosis if infected, and the benefit of therapy (Horsburgh and Rubin, Clinical practice: latent tuberculosis infection in the United States. N Engl J Med 2011; 364:1441–8). Recommendations were formulated for each of the 3 groups illustrated above. These groups are concordant with current recommendations for the interpretation of the tuberculin skin test (American Thoracic Society, Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep 2000; 49:1–51). Abbreviations: CXR, chest radiograph; HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; Mtb, Mycobacterium tuberculosis; RR, ; TB, tuberculosis; TST, tuberculin skin test.

Additional information on persons at risk for LTBI and progression to TB disease see: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):1-141;
CDC. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

Alaska Natives, particularly persons from the Southwest and Northern regions, have an increased likelihood of infection with Mtb due to the current and historic epidemiology of tuberculosis in our state.

When to Conduct Targeted Testing

Alaska has a high prevalence of prior positive tuberculin skin tests among its highest risk populations – Alaska Natives, residents of the Southwest and Northern regions of the state, the homeless, and recent immigrants. Tuberculosis screening among these groups cannot be done using tuberculin skin testing. Instead, a combination of symptom screening and sputa collection is done. Please consult the Alaska TB Program at 907-269-8000 for assistance in planning TB screening in these populations.

Targeted testing programs should be conducted only among groups, and testing should be discouraged for groups at low risk.[5] High-risk groups include persons likely to be infected with Mtb and those with increased risk for developing tuberculosis (TB).

Factors that identify persons at high risk of LTBI infection and/or progressing to TB disease are listed in **Figure 1.** Paradigm for evaluation of those with latent tuberculosis infection (LTBI) based on risk of infection, risk of progression to tuberculosis, and benefit of therapy.

Evaluate high-risk patients for LTBI as specified in the Diagnosis of Latent Tuberculosis Infection section **7.7**.

Offer treatment of LTBI to infected persons, irrespective of age, who are considered to be at high risk for developing active TB.[6] See the Treatment of Latent Tuberculosis Infection section **8.4**.

Approaches to Increasing Targeted Testing and Treatment of Latent Tuberculosis Infection

The Centers for Disease Control and Prevention (CDC) describes two approaches to increasing targeted testing and treatment of LTBI. To plan and implement programs for targeted testing and treatment of LTBI, follow the recommended approaches outlined below.[7]

One approach is to promote clinic-based testing of persons who are under a clinician's care for a medical condition (e.g., human immunodeficiency virus [HIV] infection or diabetes mellitus) that also confers a risk for acquiring TB. This approach depends on a person's risk profile for TB.[8]

The other approach is to establish specific programs that target a subpopulation of persons who have a high prevalence of LTBI or who are at high risk for acquiring TB

disease if they have LTBI, or both. This approach requires identifying the subpopulations or areas with high TB risk through epidemiologic analysis and profiling.[9]

For information on the system for prioritizing persons for targeted testing, refer to "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]:40–42) at http://www.cdc.gov/mmwr/PDF/rr/rr5412.pdf .

The US Preventive Services Task Force published recommendations for LTBI screening and treatment "Screening for Latent Tuberculosis Infection in Adults: US Preventive Services Task Force Recommendation Statement" *JAMA* . .969-962:(9)316;2016doi:10.1001/jama.2016.11046 http://jamanetwork.com/journals/jama/fullarticle/2547762

For assistance in planning targeted testing, contact the Alaska TB Program at 907-269-8000.

Screening for Latent Tuberculosis Infection in Facilities

Screening for LTBI should be conducted based upon each facility's risk for transmission of *Mycobacterium tuberculosis* (i.e., low risk, medium risk, or potential for ongoing transmission),[10] as determined in its TB risk assessment (both initial baseline assessment and periodic reassessments).

Risk assessment protocols and elements are outlined in 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 .

Screening determines if a person should be evaluated for LTBI or TB disease by asking questions to gather information about whether the person

- has signs or symptoms of TB disease;
- belongs to a group at high risk for LTBI or (if infected) for progression to TB disease; or
- has a prior positive tuberculin skin test (TST).

Alaska Program Standards for Health Care Facilities, Staff and Long Term Care Facilities

Health Care Facilities and Staff

In Alaska, health-care facilities licensed under Title 7, Chapter 12 of the Alaska Administrative Code (general acute care hospitals, specialized hospitals, nursing homes, intermediate-care facilities for the mentally retarded, ambulatory surgical facilities, birth centers, mental health centers, home health and home health agencies should have employee health programs that require each employee to be evaluated for TB within the first two weeks of employment and annually thereafter according to the Occupational Safety and Health Administration (OSHA) and/or state requirements.

See the Statutes and Regulations section for more information on:

7 AAC 12.571. Employee health program
http://www.legis.state.ak.us/basis/folioproxy.asp?url=http://wwwjnu01.legis.state.ak.us/cgi-bin/folioisa.dll/aac/query=[group+!277+aac+12!2E571!27!3A]/doc/{@1}/hits_only

7 AAC 12.650. Employee health program
http://www.legis.state.ak.us/basis/folioproxy.asp?url=http://wwwjnu01.legis.state.ak.us/cgi-bin/folioisa.dll/aac/query=[group+!277+aac+12!2E650!27!3A]/doc/{@1}/hits_only

Long Term Care Facilities

Persons being admitted to long-term care institutions who have a positive skin test (i.e., >10 mm induration) and who have not had a recent chest x-ray (within 1 month of admission) should have a chest x-ray [MMWR 1990:39(RR-10);7-20]. A person who develops protracted cough or fever or who has abnormal chest x-ray findings compatible with tuberculosis, especially if there is a significant skin test reaction, should be evaluated further (with sputum specimens for acid-fast bacilli smear and mycobacterial culture) to exclude tuberculosis.

Two-step testing improves the interpretation of tuberculin skin tests and should be used for the **initial** skin testing of adults who will be retested periodically, such as healthcare workers. See the Infection Control section for more information **(17.11)**.

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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.

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B Notifications

CONTENTS

Introduction

Purpose

Use this section to

- follow up on B1 and B2 notifications and
- evaluate and treat immigrants with B1 and B2 notifications.

B notifications are sent by the Centers for Disease Control and Prevention (CDC) to the Alaska Tuberculosis Control Program as follow-up to the 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 and refugees with Class B1 and B2 TB notification status should be given highest priority by all TB control programs.[2] Legal immigrants and refugees with Class B1 and B2 TB notification status are also a high-priority subpopulation for screening for latent TB infection (LTBI).[3]

The purpose of mandated screening is to deny entry to persons who have either communicable diseases of public health import or physical or mental disorders associated with harmful behavior, abuse drugs or are addicted to drugs, or are likely to become wards of the state.[4]

Pre-Arrival Medical Screening for Tuberculosis

Not all foreign-born persons who enter the United States go through the same official channels or through the screening process.[5] For a summary of which groups of foreign-born persons are screened, refer to Table 1: **Numbers of Foreign-Born Persons Who Entered the United States, by Immigration Category, 2002**. 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 the United States for diseases of public health significance, including TB.[6,7]

Table 1: NUMBERS OF FOREIGN-BORN PERSONS WHO ENTERED THE UNITED STATES, BY IMMIGRATION CATEGORY, 2002[8,9]

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.[10]			

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.

Overseas Screening of Applicants for Immigration

Applicants for immigration, including immigrants, refugees and asylees, who plan to relocate permanently to the United States are required to have a complete medical evaluation prior to entering the country. Additional screening recommendations for overseas panel physicians are summarized in Table 2: **Overseas Screening of Applicants for Immigration**.

Significant changes in the 2009 Technical Instructions for Tuberculosis Screening and Treatment Using Cultures and Directly Observed Therapy include requiring:

- Tuberculin skin tests (TST) or IGRA for applicants 2-14 years of age in countries with a World Health Organization (WHO)-estimated tuberculosis incidence rate ≥ 20 cases per 100,000.[11]
- A chest radiograph for all applicants >15 years of age.
- Collection of three sputum smears and cultures for Mtb..
- Completion of treatment prior to immigrating to the United States, according to American Thoracic Society/CDC/Infectious Diseases Society of America guidelines.
- Treatment under a directly observed therapy (DOT) program.

Table 2: OVERSEAS SCREENING OF APPLICANTS FOR IMMIGRATION [12,13]

Applicant age and country of origin	Medical History & Physical Examination	TST or IGRA	Chest radiograph	History, exam or CXR suggestive of TB or HIV	Three sputum smears and cultures	Drug susceptibility testing on positive culture
≥ 15 years of age in countries with WHO-estimated TB incidence <20 cases/100,000	Yes	N/A	Yes	Yes	Yes	Yes
2 - 14 years of age in countries with WHO-estimated TB incidence ≥20 cases/100,000	Yes	Yes	Yes, if TST/IGRA positive	Yes	Yes	Yes
≥ 15 years of age in countries with WHO-estimated TB incidence ≥20 cases/100,000	Yes	N/A	Yes	Yes	Yes	Yes

Sources: Centers for Disease Control and Prevention (CDC) Division of Global Migration and Quarantine (DGMQ). "CDC Immigration Requirements: Technical Instructions for Tuberculosis Screening and Treatment Using Cultures and Directly Observed Therapy". October 1, 2009. Available at: http://www.cdc.gov/immigrantrefugeehealth/pdf/tuberculosis-ti-2009.pdf and WHO. 2009 Global Tuberculosis Control Report. March 2009 no longer available on line. 2012 Global Report Available at: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf

Additional information on overseas TB screening and treatment technical instructions using cultures and DOT implementation is available at: https://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-implementation.html

Applicants who are identified as having abnormalities in their chest radiographs consistent with TB are classified according to the criteria in Table 3: **Classification of Immigrants and Refugees in the B Notification Program**. 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 enters the country with Class B2 status.[14] If abnormalities are present in a chest radiograph and if 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 follows up on medical screenings of persons with B1 and B2 classifications after their arrival in the United States.[15] 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) on entry to the United States and reported to CDC's Division of Global Migration and Quarantine (DGMQ). The DGMQ notifies state and local health departments of refugees and immigrants 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 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.[16]

Table 3: CLASSIFICATION OF IMMIGRANTS AND REFUGEES IN THE B NOTIFICATION PROGRAM[17]

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 and sputum smears are negative and apply for a waiver signed by the local health department in their intended US destination (A Waiver) or ▪ Complete TB therapy overseas
B1	Abnormal, suggestive of active TB disease	Negative	Instructed to voluntarily report to the local health department in the United 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]. August 2011. Available at: http://ctca.org/fileLibrary/file_375.pdf Accessed October 30, 2012.

Policy

Newly arrived refugees and immigrants with Class B1/B2 TB will receive thorough and timely TB evaluations and appropriate treatment to ensure prompt detection of TB disease and prevention of future cases.[18] In Alaska, public health nurses are frequently the first and only point of contact for immigrants and refugees needing clearance.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

Follow-up of B1 and B2 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:

- *TB Follow-up Worksheet*
- DS-2053: *Medical Examination for Immigrant or Refugee Application*
- DS-3024: *Chest X-Ray and Classification Worksheet*

The DGMQ sends the notifications to the Alaska TB Program. The DGMQ also sends a letter to any immigrant or refugee with a tuberculosis (TB) condition, indicating that a follow-up is needed in the United States.

The Alaska TB Program sends the notification form via mail to the public health nurse (PHN) closest to the residence listed on the form. The PHN attempts to locate the immigrant and schedule a visit either at the public health center or with a private provider (see Patient Follow-up below).

After the immigrant has been evaluated, the PHN or private provider should complete the *TB Follow-up Worksheet* and return via mail or fax to the Section of Epidemiology, Alaska TB Program, 3601 C Street, Suite 540, Anchorage, AK 99503

Section of Epidemiology, Alaska TB Program Fax Number: 907-563-7868.

A blank copy of the *TB Follow-up Worksheet* is available in the Forms Section of the Manual **(18)**

Electronic Disease Notification Process Overview

The Alaska TB Program receives notification of newly arrived immigrants, refugees and asylees electronically from the Centers for Disease Control and Prevention (CDC) through the Electronic Disease Notification (EDN) system. Records from overseas medical examinations are downloaded and sent to local public health centers.

The PHN ensures the evaluation of the new arrival and returns a completed Follow-*Up Worksheet to* the Alaska TB Program via mail or fax. Follow-up worksheets may need to be submitted more than once: upon initial completion of the medical evaluation for tuberculosis; when culture results come back; and when therapy for active disease or latent tuberculosis infection is completed.

If the local PHN 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 Alaska TB Program with an explanation as to why the evaluation was unable to be completed.

At the Alaska TB Program a designated staff member enters data from the returned *TB Follow-up Worksheet* into the Electronic Disease Notification database and submits it to the CDC. The Alaska TB Program tracks the status of the evaluation of each new arrival and will contact local PHNs about missing or incomplete “TB Follow-up Worksheets”.

Patient Follow-up

The immigration paperwork may make it appear that a patient has had a complete evaluation for TB disease. However, the overseas evaluation is designed only to detect abnormal radiographs and determine infectiousness at the time of travel and does not rule out disease. Remember that all B1 and B2 arrivals need a new diagnostic evaluation for active disease, including a tuberculin skin test and new chest radiograph. Even if active TB disease is ruled out, most B1 and B2 arrivals are priority candidates for treatment of latent TB infection.

Follow-up on each B1 and B2 arrival is described below.

1. Check to see if the immigrant has already visited the public health center or a private provider.
2. If not, then make a telephone call to the home of the immigrant’s sponsor or relative within five business days after receiving the notification. Arrange for the immigrant to come in during clinic hours at the public health center and/or arrange for the patient to see a private provider. Whenever possible, communications should be made in the immigrant’s first language.
3. If the immigrant does not visit the public health center or a private provider within 10 business days (two weeks) of the telephone call, send a letter to the home of the immigrant’s sponsor or relative. Whenever possible, communications should be made in the immigrant’s first language.
4. If the immigrant does not visit the public health center or a private provider within 10 business days (two weeks) of the letter, make a visit to the home of the immigrant’s sponsor or relative. Take a representative who speaks the immigrant’s first language if at all possible (if needed).
5. Every effort should be made to locate B1 or B2 arrivals as these immigrants are considered high risk for TB disease. Call the Alaska TB Program for consultation when an immigrant is not located.
6. Complete Class B follow-up within one month.
7. Be sure to indicate the final TB Diagnostic Classification in *D3. Diagnosis on the TB Follow-up Worksheet. .* Refer to Table 4 for additional information.

8. Complete and return the *TB Follow-up Worksheet* to the Alaska TB Program. This form is essential for the Alaska TB Program to conduct statewide surveillance and follow-up on all B1 and B2 arrivals and report results to the CDC.

Table 4: TB Diagnostic Classification[19]

Classifications of Persons Exposed to and/or Infected with *M. tuberculosis*	Description	Comments
Class 0	No TB Exposure	• Negative reaction to tuberculin skin test or IGRA • No history of exposure
Class 1: TB exposure, no evidence of infection	Exposure to TB but not latent TB Infection	• Negative reaction to tuberculin skin test or IGRA • No evidence of infection. • History of exposure to tuberculosis but negative reaction to the tuberculin skin test
Class 2: TB infection, no disease	Latent TB Infection	• Positive reaction to the tuberculin skin test • Negative microscopy/bacteriology results • No clinical or radiographic evidence of tuberculosis
Class 3: TB, active disease	Active TB disease	• Clinically active tuberculosis • Person must have clinical and/or radiologic evidence of tuberculosis o Established most definitively by isolation of *M. tuberculosis* o In absence for a positive culture for *M. tuberculosis*, person in this class must have a positive reaction to the tuberculin test • Class 3 is further defined as pulmonary, extra-pulmonary, both sites on the follow-up form.
Class 4: Tuberculosis, inactive disease	Old, healed, inactive TB disease	• History of previous episode(s) of tuberculosis or abnormal stable radiographic findings • Positive reaction to tuberculin skin test • Negative microscopy/bacteriology • No clinical and/or radiographic evidence of current disease[20]

Evaluation of B1, B2, and B Tuberculosis Arrivals

Evaluation Activities

B1 arrivals had negative sputum acid-fast bacilli results overseas and have overseas chest radiographs that are abnormal and suggestive of **active TB disease**

B2 arrivals had negative sputum acid-fast bacilli results overseas and have overseas chest radiographs that are abnormal and suggestive of **inactive TB disease**.

Highlights of the major changes to the 2008 "Tuberculosis Component of the Technical Instructions for the Medical Examination of Aliens in the United States"[21] include:
:

- **Sputum cultures for *M. tuberculosis*, and drug susceptibility testing for positive cultures, are required for applicants with chest radiograph findings suggestive of active TB disease.**

- **Applicants with Class A (either smear or culture positive) TB must complete a full course of TB treatment.** Completion of therapy is required prior to medical clearance for TB by the civil surgeon, for purposes of this examination and the United States Immigration and Citizenship Services (USCIS).

- **A chest radiograph is required for all applicants with a tuberculin skin test (TST) reaction of 5 mm or greater of induration, including pregnant (or possibly pregnant) women.**

- **A chest radiograph is now required for applicants with a TST reaction of less than 5 mm of induration (including no induration) who have:**
    - **Signs or symptoms** consistent with active TB disease.
    - **Immunosuppression** for any reason (e.g., HIV+; immunosuppressive therapy $\geq$ 15 mg/day of prednisone for one month or longer; or history of organ transplantation).

- **Definitions of chest radiograph findings** that are suggestive of TB disease are provided to assist in determining the proper TB classification.

- **A new TB classification (Class B: Latent TB Infection Needing Evaluation for Treatment)** should be used for all applicants who are recent arrivals to the United States (less than 5 years) from countries with a high TB prevalence, with a TST reaction of $\geq$ 10 mm induration, and no evidence of TB disease.

Refer to Table 5: **Evaluation and Follow-Up Recommendations for B1, B2, And B Tuberculosis Arrivals in Alaska** to determine which evaluation tasks should be done.

Table 5: EVALUATION AND FOLLOW-UP RECOMMENDATIONS FOR B1, B2, AND B TUBERCULOSIS ARRIVALS IN ALASKA[22]

Classification	Overseas Diagnostic Criteria	TB Follow-up Recommendations
Class B1 TB – Pulmonary TB, Active, Non-infectious	• Abnormal, chest radiograph suggestive of active TB • Three sputum smears negative for AFB and three cultures negative for *MTB*	□ Review TB treatment history. □ Evaluate for signs and symptoms of TB. □ Do TST or IGRA regardless of BGC history, unless reliable documentation of previous positive test. Induration of ≥ 5 mm is positive in persons with abnormal chest radiographs. □ Do CXR regardless of TST/IGRA result, or if overseas CXR done ≥ 3 months ago. Submit films for review. □ Collect three sputa for AFB and culture, to determine TB diagnosis (i.e. LTBI, inactive or active TB).
Class B1 TB – Extrapulmonary TB, Active, Non-infectious	• Radiographic or other evidence of extrapulmonary TB; no pulmonary TB	□ Review TB treatment history. □ Evaluate for signs and symptoms of TB. □ Do TST or IGRA regardless of BGC history, unless reliable documentation of previous positive test. Induration of ≥ 5 mm is positive in persons with abnormal chest radiographs. □ Do CXR regardless of TST/IGRA result, or if overseas CXR done ≥ 3 months ago. Submit films for review. □ Collect three sputa for AFB and culture, to determine TB diagnosis (i.e. LTBI, inactive or active TB).
Class B2 TB – Pulmonary TB, Inactive, Non-infectious	• Abnormal chest radiograph suggestive of inactive TB disease • No sputum AFB smears or cultures required	□ Review TB treatment history. □ Evaluate for signs and symptoms of TB. □ Do TST or IGRA regardless of BGC history, unless reliable documentation of previous positive test. Induration of ≥ 5 mm is positive in persons with abnormal chest radiographs. □ Do CXR regardless of TST/IGRA result, or if overseas CXR done ≥ 3 months ago. Submit films for review. □ Collect three sputa for AFB and culture, to determine TB diagnosis (i.e. LTBI, inactive or active TB).
Class B – Latent TB Infection needing evaluation for treatment (LTBI)	• TST reaction ≥ 10 mm in recent U.S. arrivals • TST reaction ≥ 5 mm in specific groups • No evidence of active TB disease	□ Consider patient to have LTBI. Evaluate for signs and symptoms of TB. □ Consider repeat TST or IGRA, if indicated, to confirm or rule-out overseas diagnosis of LTBI. □ Do CXR if overseas CXR done > 3 months ago or if HIV+. □ Collect three sputa for AFB and culture, if symptomatic, to rule out active TB disease. □ Offer treatment for LTBI after provider evaluation.

Source: Adapted from Centers for Disease Control and Prevention (CDC). "2008 Tuberculosis Component of Technical Instructions for the Medical Examination of Aliens in the United States". Available at http://www.cdc.gov/immigrantrefugeehealth/pdf/tb-ti-civil.pdf

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.* If sputa have been collected, wait for final negatyive culure before initiating LTBI treatment. B1/B2 immigrants with positive tuberculin skin tests and 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 is based on 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 using a combined pill, Rifamate (if available) or with nine months of isoniazid.[23]

For more information on treatment, see the Treatment of Latent Tuberculosis Infection **(8.2)** and Treatment of Tuberculosis Disease **(6.2)** sections.

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 A/B” *(CDHS/CTCA Joint Guidelines;* 2011). Available at: http://ctca.org/fileLibrary/file_375.pdf
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- U.S. Department of Health and Human Services (DHSS) Public Health Service (PHS) Centers for Disease Control and Prevention (CDC) National Center for preparedness Detection and Control of Infectious Disease Division of Global Migration and Quarantine (DGMQ). “Tuberculosis Component of Technical Instructions for the Medical Examination of Aliens in the United States”. May 2008. Available at: http://www.cdc.gov/immigrantrefugeehealth/pdf/tb-ti-civil.pdf

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Diagnosis of Tuberculosis Disease

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska guidelines to

- 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; and
- 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 **11.1**. For information on treatment, refer to the Treatment of Tuberculosis Disease section **6.1**.

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 or nucleic acid amplification (NAA) tests 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 or NAA 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.

Policy

In Alaska:

- Persons who show or report signs and symptoms of TB should be; 1) evaluated for TB disease as described in the "Diagnosis of Tuberculosis Disease" topic in this section and 2) reported as suspected cases of TB as described in the "Reporting Tuberculosis" topic in the Surveillance section **2.6**.
- Contacts should be evaluated as described in the Contact Investigation section **11.1**.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction section **1.18***.*

Reports of suspected or confirmed tuberculosis should be made as soon as possible and must be made within 5 working days after first diagnosing or suspecting the existence of the disease.

Forms

Reporting forms and information are available in the Forms section **(18.1)** or at http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.aspx

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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[7]

Class	Type	Description
0	▪ No tuberculosis (TB) exposure ▪ Not infected	▪ No history of exposure ▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	▪ TB exposure ▪ No evidence of infection	▪ History of exposure ▪ Negative reaction to the TST or IGRA
2	▪ TB infection ▪ No disease	▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) ▪ No clinical, bacteriologic, or radiographic evidence of TB disease
3	▪ TB disease ▪ Clinically active	▪ *Mycobacterium tuberculosis* complex cultured (if this has been done) ▪ Clinical, bacteriologic, or radiographic evidence of current disease
4	▪ TB disease ▪ Not clinically active	▪ History of episode(s) of TB Or ▪ Abnormal but stable radiographic findings ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) And ▪ No clinical or radiographic evidence of current disease
5	▪ TB suspect	▪ Diagnosis pending

Source: Adapted from: CDC. Classification system. In: Chapter 2:Transmission and Pathogenesis of Tuberculosis. *Core Curriculum on Tuberculosis: What the Clinician Should Know (2016)* [Division of Tuberculosis Elimination Web site]. Updated May 2016. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf . Accessed January 10, 2017.

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 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease** should be targeted for tuberculin skin testing in Alaska.

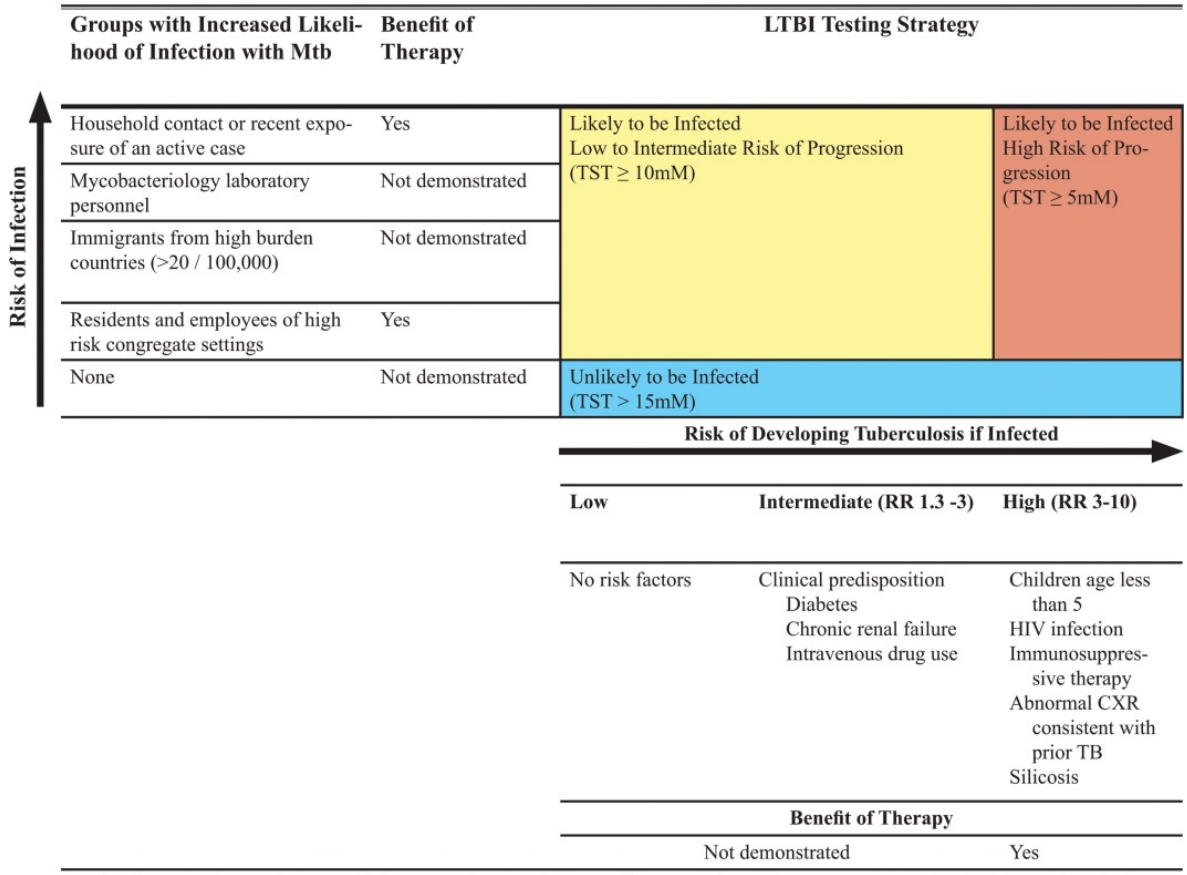
Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country with HIV infection is at much higher risk of having active TB than a US-born individual with HIV infection.

Table 2: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE[8]

For Tuberculosis Infection	For Progression to Tuberculosis Disease[9]
▪ High-priority contacts such as housemates or coworkers or contacts of persons who have smear-positive pulmonary or laryngeal TB ▪ Infants, children, and adolescents exposed to adults in high-risk categories ▪ Recent immigrants (<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 here are occurring among immigrants from those countries) ▪ Recent immigrants from Mexico ▪ Migrant workers ▪ Persons who have recently spent over 3 months in high-incidence countries (such as missionaries)) ▪ Persons with high rates of TB transmission: • Homeless persons • Substance users • Persons with human immunodeficiency virus (HIV) infection • Persons living or working in institutions with individuals at risk for TB such as: ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities ▪ Alaska-specific risk includes persons from the Southwest and Northern regions of the state and Alaska Natives	▪ 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 who smoke cigarettes ▪ 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., leukemias 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.

Figure 1. PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY[10]



In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Figure 1. In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to tuberculosis if infected, and the benefit of therapy (Horsburgh and Rubin, Clinical practice: latent tuberculosis infection in the United States. N Engl J Med 2011; 364:1441–8). Recommendations were formulated for each of the 3 groups illustrated above. These groups are concordant with current recommendations for the interpretation of the tuberculin skin test (American Thoracic Society, Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep 2000; 49:1–51). Abbreviations: CXR, chest radiograph; HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; Mtb, Mycobacterium tuberculosis; RR, ; TB, tuberculosis; TST, tuberculin skin test.

Case Finding

Identifying Suspected Tuberculosis Cases

Most 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.[11] Professionals in the primary healthcare sector, including hospital and emergency department clinicians, should be trained to recognize patients with symptoms consistent with TB.[12]

- Be alert for cases of TB among:
    - Persons who are contacts of patients with pulmonary TB
    - Persons with newly diagnosed infection with *Mycobacterium tuberculosis* (sometimes referred to at TB skin test converters).
- Screening for TB disease is especially important for: [13]
    - Immigrants and refugees with Class B1 or Class B2 TB notification status See B Notifications section **4.1**.
    - Persons involved in TB outbreaks, and occasionally in working with populations with a known high incidence of TB.
    - When the risk for TB in the population is high and
    - Persons in jails, prisons, and other congregate facilities.

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 two to three weeks, or other compatible signs and symptoms.[14]

Note that these symptoms should suggest a diagnosis of TB but are not required. TB should be considered a diagnosis in asymptomatic patients with chest radiographs compatible with TB.

Table 3: WHEN TO SUSPECT PULMONARY TUBERCULOSIS IN ADULTS[15]

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†,[16]
Signs and Symptoms Typical of TB	▪ Prolonged coughing (≥2–3 weeks) with or without production of sputum that might be bloody (hemoptysis)§,[17] ▪ Chest pain[18] ▪ Chills[19] ▪ Fever ▪ Night sweats ▪ Loss of appetite[20] ▪ Weight loss ▪ Weakness or easy fatigability[21] ▪ Malaise (a feeling of general discomfort or illness)[22]
Chest Radiograph: Immunocompetent patients	▪ Classic findings of TB are upper-lobe opacities, frequently with evidence of contraction fibrosis and cavitation¶
Chest Radiograph: Children and patients with advanced HIV infection	▪ Lower-lobe and multilobar opacities, hilar adenopathy, or interstitial opacities might indicate TB

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

† 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, 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.

Follow-up on Suspected Cases of Tuberculosis

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

When a suspected case of pulmonary TB is identified, refer to Table 4: **Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios** in the "Diagnosis of Tuberculosis Disease" topic in this section **5.11**. 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.[23]

To report a suspected or confirmed case of TB, call the Alaska TB Program at 907-269-8000, or after hours, at 800-478-0084. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[24]

The patient should be masked and immediately excluded from the workplace, school and social activities and if hospitalized should be placed in airborne infection isolation (AII) until confirmed noninfectious. For more information, see the "Isolation" topic in the Infection Control section of this manual **17.15**.

Laboratories should report positive smears, NAA or positives cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the Alaska TB Program, as specified in the "Reporting Tuberculosis" topic in the Surveillance section **2.6**.

Within 48 hours of suspect identification, administer a tuberculin skin test (TST) or IGRA and obtain a chest radiograph. Evaluate the patient for TB disease as specified in the "Diagnosis of Tuberculosis Disease" topic in this section.

- In remote locations patients may begin TB treatment based upon history, clinical findings, and smear results.
- Individuals who require commercial air transport to a medical facility for a chest radiograph should **not** travel until they are noninfectious. This generally requires completion of 14 days of TB medications; clinical improvement and three (3) consecutive negative AFB smear results.

When managing TB suspects or cases in remote villages and communities, please consult the Alaska TB Program at 907-269-8000 for guidance.

Diagnosis of Tuberculosis Disease

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 or interferon gamma release assay
- Chest radiography
- Bacteriologic examination

When a suspected case of pulmonary TB is identified, refer to Table 4 for guidelines for the initial steps of TB case detection in five clinical scenarios encountered by primary care providers and emergency physicians.[25]

Table 4: GUIDELINES FOR THE EVALUATION OF PULMONARY TUBERCULOSIS IN ADULTS IN FIVE CLINICAL SCENARIOS[26]

Patient and Setting	Recommended Evaluation
Any patient with a cough of ≥2–3 weeks' duration	Chest radiograph and collect 3 sputum specimens for acid-fast bacilli (AFB) smear microscopy and culture[27] Note: Where chest radiography is not available, collect 3 sputum specimens for AFB smear microscopy and culture
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms of ≥2–3 weeks' duration†	Chest radiograph and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA. Note: Where chest radiography is not available, collect 3 sputum specimens for AFB smear microscopy, culture and NAA
Any patient with human immunodeficiency virus (HIV) infection and unexplained cough or fever	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy and culture
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
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 and culture

* Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.[28]
† See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease (5.6).
§ 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 3: **When to Suspect Pulmonary Tuberculosis in Adults [5.8],** Table 4: **Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios [5.11],** and Table 5: **Symptoms of Tuberculosis Disease [5.12]**).
- Previous TB infection or disease and history of treatment with anti-TB medications
- Risk factors (as listed in Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease [5.6])**
- 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) or Alaska-specific risk factors such as residing in the Southwest or Northern regions of the state, being Alaska Native or experiencing homelessness.

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 5 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 3: **When to Suspect Pulmonary Tuberculosis in Adults 5.8**.

Table 5: SYMPTOMS OF TUBERCULOSIS DISEASE[29]

Pulmonary	General: Pulmonary and Extrapulmonary	Extrapulmonary
▪ Coughing ▪ Coughing up sputum or blood ▪ Pain in the chest when breathing or coughing	▪ Chills[30] ▪ Fever ▪ Night sweats ▪ Loss of appetite[31] ▪ Weight loss ▪ Weakness or easy fatigability[32] ▪ Malaise (a feeling of general discomfort or illness)[33]	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.

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.

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, how the disease was treated, and how long they took medications. 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** 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. See Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease (5.6)**.[34] For persons previously skin tested, an increase in induration of 10 mm within a two-year period is classified as a conversion to positive.

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

For a list of behaviors and conditions that appear to increase the risk that TB infection will progress to disease, see Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease (5.6)**.

Human Immunodeficiency Virus Screening and Hepatitis Screening

Counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. Contacts at high risk for HIV infection should also be considered voluntary HIV counseling and testing.[35]

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

- Routine HIV screening for all patients ages 13–64 seeking health care for any reason, without regard to any patient's known risks for HIV infection
- Annual HIV screening of patients known to be at high risk[36]
- All patients in TB Clinics should be tested for HIV. This includes persons with TB disease or LTBI.[37]

- All patients with a history of injecting drug use, birth in Asia or Africa (or other hepatitis virus endemic regions), or who have HIV should have baseline testing for hepatitis B and C.[38]

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 presents; and the presence of extrapulmonary TB.[39]

Tuberculin Skin Test and Interferon Gamma Release Assays

Use the Mantoux TST to test for *M. tuberculosis* infection in persons who do not have a previous positive TST. Note that for patients with a previous documented positive TST reaction, a TST is not necessary. 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 IGRA currently approved by the Food and Drug Administration (FDA) and available on the market is QuantiFERON®-TB Gold (QFT-G), which can be used in all circumstances in which the TST is used. QFT-G usually can be used in place of the TST.[40] 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.[41] **At the present time, IGRA testing is only available through private laboratories in Alaska. The Alaska TB Program does not provide or pay for IGRA testing.**

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. In addition, the IGRA test appears to be less affected by past bacille Calmette-Guérin (BCG) vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results. However, the IGRA test has practical limitations that require that blood collected is handled, incubated and processed according to test-specific protocols.[42]

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

Persons with a positive TST or IGRA 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.

A negative TST does not rule out TB disease—as many as 20% of patients with TB disease have a negative TST reaction.[43] 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.[44]

For more information on the Mantoux TST, see the Diagnosis of Latent Tuberculosis Infection section **7.2**. 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.

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. See Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 16 years of age) **9.1**

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* (2011) at

http://currytbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-04

Bacteriologic Examination

Refer to Table 6 below to determine the types of specimens needed to assist in the diagnosis of TB.

Table 6: SPECIMENS FOR DIAGNOSING TUBERCULOSIS DISEASE

Suspected Diagnosis	Specimen Needed
Pulmonary or laryngeal tuberculosis (TB)	Three morning sputum (phlegm from deep in the lungs) samples for TB 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 (heparinized)

CDC recommends the use of a rapid molecular test (NAA or GeneXpert) on at least one (1) specimen from each patient with signs and symptoms of pulmonary tuberculosis for whom a diagnosis of tuberculosis is being considered but has not been established, and for whom the test result would alter case management or tuberculosis control activities.[46]

Weblink:
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm?s_cid=mm5801a3

Contact the Alaska TB Program at 907-269-8000 to request molecular testing for patients meeting these criteria. Refer to Table 7 below for information on the

bacteriology tests used to diagnose TB.

Table 7: BACTERIOLOGY TESTS USED IN DIAGNOSING TUBERCULOSIS DISEASE[47]

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).	▪ On-site test: within 24 hours from specimen collection. ▪ Off-site test: within 24 hours from laboratory receipt of specimen (time from specimen collection to laboratory receipt should be 24 hours or less).[48]
Nucleic Acid Amplification (NAA) Test [49]	▪ A test done on clinical 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.[50]	GeneXpert® Xpert® MTB/RIF Assay: ▪ On-site test: within 24 hours from specimen collection Off-site test: within 24-48 hours from laboratory receipt of specimen [51,52] TB PCR ▪ Off-site test: within 24-48 hours from laboratory receipt of specimen
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 [53,54]
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.[55,56]	▪ First-line drugs (ASPHL): within 15 days from identification ▪ Second-line drugs (Reference lab): 4 weeks from laboratory receipt of isolate

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 should report positive smears, cultures, NAA or GeneXpert results and primary healthcare providers should report suspected or confirmed cases of TB to the health department, as specified in the “Reporting Tuberculosis” topic in the Surveillance section. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[57]

For information on reporting, see the “Reporting Tuberculosis” topic in the Surveillance section **2.6**.

For a list of all of the laboratory services available and information on specimen collection and shipment, see the Laboratory Services section **(12.1)** or visit: http://dhss.alaska.gov/dph/Labs/Pages/publications/default.aspx

Resources and References

Resources

- ATS, CDC, IDSA. “Diagnosis of Tuberculosis in Adults and Children” (*Clinical Infectious Diseases 2017*;64[2]:1-33). Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/cid_ciw694_full.pdf
- CDC. *Self-Study Modules 1 – 9 on Tuberculosis* (Division of Tuberculosis Elimination Web site; 2016). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm
- CDC. *Core Curriculum on Tuberculosis (2013)* (Division of Tuberculosis Elimination Web site; updated October 2013). Available at: http://www.cdc.gov/tb/education/corecurr/default.htm
- Tenover, R., et al. “The Resurgence of Tuberculosis: Is Your Laboratory Ready?” (*Journal of Clinical Microbiology* 1993:767–770). Available at: http://jcm.asm.org/content/31/4/767.full.pdf

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[3] 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):32.
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Treatment of Tuberculosis Disease

CONTENTS

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 Alaska guidelines to

- 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; and
- 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.[1]

Policy

Patients with TB disease in Alaska or who move to Alaska with reported TB disease should receive and complete treatment in accordance with the national guidelines set forth in this manual and in accordance with Alaska laws and regulations.

State Laws and Regulations

AS 18.15.380. Medical treatment

A health care practitioner or public health agent who examines or treats an individual who has or may have been exposed to a contagious disease shall instruct the individual about the measures for preventing transmission of the disease and the need for treatment. The Alaska Department of Health and Social Services may administer treatment, including the use of directly observed therapy where appropriate, to a consenting individuals who has or may have been exposed to a contagious disease. An individual has the right to refuse treatment if they are willing to take steps outlined by the state medical officer to prevent the spread of communicable disease to others.

See the Statutes and Regulations section of this manual **(19.1)** or *Conditions Reportable to Public Health*, pages 19-40, available at: http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/ConditionsReportable.pdf

Program Standards

- Persons with newly diagnosed TB, for whom therapy for $\leq$ 1 year is indicated, will complete therapy within 12 months.
- Persons with newly diagnosed pulmonary TB will receive an ATS/IDSA/CDC recommended treatment regimen.[2]
- All persons with pulmonary tuberculosis will receive treatment using directly observed therapy (DOT).

*ATS – American Thoracic Society; IDSA – Infectious Disease Society of America; CDC – Centers for Disease Control and Prevention

Forms

See *Conditions Reportable to Public Health* for forms and instructions on how to report suspected or confirmed cases of tuberculosis in Alaska. It is available at: http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/ConditionsReportable.pdf

For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction **1.18**.

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). 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.
	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 health care provider who is licensed in the State of Alaska.
	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 3 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 the number of full weeks of treatment , not solely on the duration of therapy.

Treatment Regimens and Dosages

Use this information to:

- identify the appropriate regimen;
- determine the appropriate dosage for each drug; and
- 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" topic in this section 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; or when the patient is pregnant or breastfeeding.

For detailed information on the treatment of tuberculosis in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 15 years of age) section **9.1**.

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).

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: **Four Treatment Regimens for Drug-Susceptible Tuberculosis**, the initial phase is denoted by a

number (1, 2, 3, or 4) according to effectiveness of the regimen with regimen 1 having the greatest effectiveness.

Ethambutol helps to prevent rifampin resistance when primary isoniazid resistance is present. Ethambutol can be discontinued as soon as once drug susceptibility results are known and the organisms are fully susceptible.[3]Pyrazinamide has potent sterilizing ability which allows shortening the regimen from 9 months to 6 months when two (2) months of PZA are included in the 2-month initial phase of treatment. See Table 3: **Four Treatment Regimens for Drug-Susceptible Tuberculosis** for additional information.

Directly observed therapy (DOT) is the standard of care for all persons with tuberculosis. It is required for all persons being treated for pulmonary tuberculosis.

The recommended regimens, and the number of doses specified by each regimen, are described in Table 3. Providers writing prescriptions for anti-TB medications and PHNs ordering these medications should use this reference to determine how many doses of each drug should be ordered from the SOE Drug Room.

For detailed information on the treatment of tuberculosis in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 15 years of age) section 9.1.

For consultation regarding the treatment of TB, contact the Alaska TB Program at 907-269-8000.

When using three times weekly doses of TB medications, doses should be scheduled on Monday, Wednesday and Friday to avoid long intervals between doses.

Table 3: DRUG REGIMENS FOR MICROBIOLOGICALLY CONFIRMED PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS

Intensive Phase			Continuation Phase				
Regimen	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182-130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk(	110-94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve	
3	INH RIF PZA EMB	3 times weekly for 24 does (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior	Lesser

Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

Abbreviations: DOT: directly observer therapy; EMB: ethambutol; HIV: human immunodeficiency virus; INH: isoniazid; PZA: pyrazinamide; RIF: rifampin

[a] Other combinations may be appropriate in certain circumstance; additional details are provided in the section "recommended Treatment Regimens."

[b] When DOT is used, drugs may be given 5 days per 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. DOT should be used when drugs are administered <7 days per week.

[c] Based on expert opinion, patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31-week) continuation phase

[d] Pyridoxine (vitamin B6), 25-50 mg/day, is given with INH total persons at risk of neuropathy(eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advance age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

[e] Alternatively, some US tuberculosis control programs have administered intensive-phase regimens 5 days per week for 15 doses (3 weeks), then twice weekly for 12 doses.

Dosages

Once the appropriate regimen has been identified, refer to Table 4: **Doses of First-line Antituberculosis Drugs for Adults and Children** for instructions on dosages for each drug. First-line antituberculosis medications should be administered together; split dosing should not be used

The following drugs are available in the state of Alaska for treating TB disease. These drugs are provided free of charge upon approval of the TB Program.

- Isoniazid (INH)
- Rifampin (RIF)
- Rifabutin (RFB)
- Rifapentine (RPT)
- Ethambutol (EMB)
- Pyrazinamide (PZA)
- Aminoglycoside (amikacin, streptomycin)
- Moxifloxacin

For information regarding second-line drugs, contact the Alaska TB Control Officer at 907-269-8000.

Daily dosing (5 days/week) is preferred during the initiation phase of treatment and should be used during the continuation phase whenever possible. If daily dosing is not an option, three (3) times weekly dosing should be used. Twice weekly dosing is the least effective of the approved treatment regimens.

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

Drug	Preparation	Adult/Child	Daily	Once-weekly (1x/week)	Twice-weekly (2x/week)	Thrice-weekly (3x/week)
Isoniazid	Tablets (50, 100, 300 mg); Elixir (50 mg/5 ml); Aqueous IV/IM solution (100 mg/ml)[±]	Adults	5 mg/kg (Typically 300 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (900 mg)	15 mg/kg (typically 900 mg)
		Children	10-15 mg/kg	----	20-30 mg/kg	----[†]
Rifampin	Capsule (150, 300 mg); suspend powder for PO; Aqueous IV solution	Adults**	10 mg/kg (typically 600 mg)	----	10 mg/kg (typically 600 mg)	10 mg/kg (600 mg)
		Children	10-20 mg/kg	----	10-20 mg/kg	----[†]
Rifabutin[††]	Capsule (150 mg)	Adults**	5 mg/kg (typically 300 mg)	----	Not recommended	Not recommended
		Children	Appropriate dosing for children is unknown. Estimated at 5mg/kg.			
Pyrazinamide	Tablet (500 mg)	Adults	40-55 kg → 1,000 mg 56-75 kg → 1,500 mg 76-90 kg → 2,000 mg	----	40-55 kg → 2,000 mg 56-75 kg → 3,000 mg 76-90 kg → 4,000 mg	40-55 kg → 1,500 mg 56-75 kg → 2,500 mg 76-90 kg → 3,000 mg
		Children	35 (30-40) mg/kg	----	50 mg/kg	----[†]
Ethambutol	Tablet (100 and 400 mg)	Adults	40-55 kg → 800 mg 56-75 kg → 1,200 mg 76-90 kg → 1,600 mg	----	40-55 kg → 2,000 mg 56-75 kg → 2,800 mg 76-90 kg → 4,000 mg	40-55 kg → 1,200 mg 56-75 kg → 2,000 mg 76-90 kg → 2,400 mg
		Children	20 (15-25) mg/kg	----	50 mg/kg	----[†]

Daily and thrice weekly dosing is preferred. See Table 3.

Abbreviation: FDA: US Food and Drug Administration; IM: intramuscular; IV: intravenous; PO:

*Dosing based on actual weight is acceptable in patients who are not obese. For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW (IBW + [0.40 x (actual weight – IBW)] as is done for initial aminoglycoside doses. Because tuberculosis drug dosing for obsess patients has not been established, therapeutic drug monitoring may be considered for such patients.

† For purpose of this document, adult dosing begins at age 15 years or at a weight of >40 kg in younger children. The optimal doses for thrice-weekly therapy in children and adolescents have not been established. Some experts use in adolescents the same doses as recommended for adults, and for younger children the same doses as recommended for twice-weekly therapy .

±Pyridoxine (vitamin B6), 20-50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism. Malnutrition, or chronic renal failure; patients with advanced age.) For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/d.

** Higher doses of rifampin, currently as high as 35 mg/kg, are being studied in clinical trials/

†† Rifabutin dose may need to be adjusted when used with protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

Duration of Treatment

The four recommended regimens for treating patients with TB caused by drug-susceptible organisms have a duration of six to nine months. Each regimen has an initial phase of two months, followed by a continuation phase of either four or seven months.

The standard duration of treatment for pulmonary TB should be six months unless **both** cavitation is present **and** the patient is still culture positive after two months, in which case nine months is recommended. Note that there are three 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.[4]
2. Treatment for bone or joint TB may need to extend to nine months.[5]
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.[6] However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of six months.[7]

In addition to patients who have cavitation on initial chest radiograph and who have positive cultures at the completion of two (2) months of treatment, an extended continuation phase of 7 months should be considered in the following situations:

- Cavitation or positive cultures at 2 months of treatment by DOT
- Body weight > 10% below ideal body weight
- Active cigarette smoking
- Diabetes
- HIV infection
- Other immunosuppressing conditions
- Extensive disease on chest radiograph[8]

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 at initiation of tuberculosis treatment and repeated as indicated by clinical signs and symptoms. See Table 5**: 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.[9]

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.[10] 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.[11] In addition, proper management of more serious adverse reactions often requires expert consultation.[12]

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

Basic Monitoring Steps

1. 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. Follow the national monitoring guidelines identified in the current guidelines for treatment of TB, “Treatment of Drug-Susceptible Tuberculosis” (ATS, CDC, IDSA.. *Clinical Infectious Diseases 2016*; 63(7):147-95.) at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .
   b. Check for guideline updates posted on the CDC’s Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/publications/guidelines/default.htm and the list of guidelines by date at: http://www.cdc.gov/tb/publications/guidelines/List_date.htm
2. While on treatment, all patients should be evaluated in person whenever possible, at baseline (before starting treatment) and then at least monthly for side effects and adverse reactions.

a. In remote locations in Alaska, monitoring may be done by telephone, however all patients should be evaluated in person at least once during their treatment regimen.

b. Patients who are potentially infectious, and must fly by a commercial conveyance into regional health care hubs for evaluation and/or chest x-ray should receive at least 2 weeks of treatment prior to traveling. Patients are considered to be non-infectious and safe to travel when they are three (3) negative AFM sputum smears and clinical improvement in addition to 2 weeks of antituberculosis treatment.

3. The common side effects of and adverse reactions to drugs used to treat TB disease are listed in Table 6: **Reporting Reactions to Antituberculosis Medications**. Educate patients to first stop the medicine and then promptly report any of the symptoms or signs listed in Table 6 or any unexplained illness to the prescribing provider immediately.

a. If a patient reports a potentially serious adverse reaction, call the patient's provider immediately and alert the Alaska TB program by calling 907-269-8000.

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 5: **Monitoring and Interventions for Side Effects and Adverse Reactions** .

b. Consult with the Alaska TB Program by calling 907-269-8000.

If you suspect that an antituberculosis drug may be interacting with other medications that the patient is taking, refer to pages 168–70 in the "Treatment of Drug-Susceptible Tuberculosis" (ATS, CDC, IDSA.. *Clinical Infectious Diseases 2016*; 63(7):147-95.) at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .

5. 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

Table 5: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS[13,14,15]

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), 25-50 mg/day, is given with INH total persons at risk of neuropathy(eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advance age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.[16] 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.

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 "Table 8: Clinically Significant Drug-Drug Interactions Involving the Rifamycins" page 10 in "Treatment of Tuberculosis" at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .[17] 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. For detailed information on the use of Rifabutin for HIV-infected patients refer to "Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents" https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/325/tb 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). 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 "Table 8: Clinically Significant Drug-Drug Interactions Involving the Rifamycins" page 10 in "Treatment of Tuberculosis" at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf.[18] Link above is 2003

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 Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.; 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. Chapter 6: Treatment of Tuberculosis Disease. *Core Curriculum on Tuberculosis (2013)* [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter6.pdf . Accessed January 18, 2017.

Reporting Reactions

The table below is intended for use by providers and public health nurses who perform case management services. Instruct the patient to report any side effects and adverse reactions listed in Table 6.

If a patient reports an adverse reaction, the provider or PHN case manager should alert the Alaska TB program by calling 907-269-8000.

Table 6: 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
*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 Drug-Susceptible Tuberculosis" (ATS, CDC, IDSA.. *Clinical Infectious Diseases 2016*; 63(7):147-95.), at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.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]. November 2011. Available at: . http://www.ctca.org/fileLibrary/file_238.pdf . Accessed January 12, 2017.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 5**: Monitoring and Interventions for Side Effects and Adverse Reactions** to

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

Response to Treatment

For consultation regarding a patient's response to treatment, contact Alaska Tuberculosis Program at 907-269-8000.

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 two 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 two months.

Radiographic evaluations during treatment are of less importance than sputum evaluation. However, a chest radiograph may be obtained at completion of treatment to provide 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 three months, a tuberculosis (TB) medical expert should be consulted. Contact the Alaska Tuberculosis Control Officer at the Alaska TB Program at 907-269-8000 immediately.

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.[20]

Completion of Therapy

A full course of therapy (completion of treatment) is determined more accurately if the total number of doses ingested and full weeks of treatment are taken into account, as well as the duration of therapy. If there are no interruptions in drug administration, six 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.[21]

For consultation regarding the treatment of tuberculosis (TB) in a patient with negative cultures, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

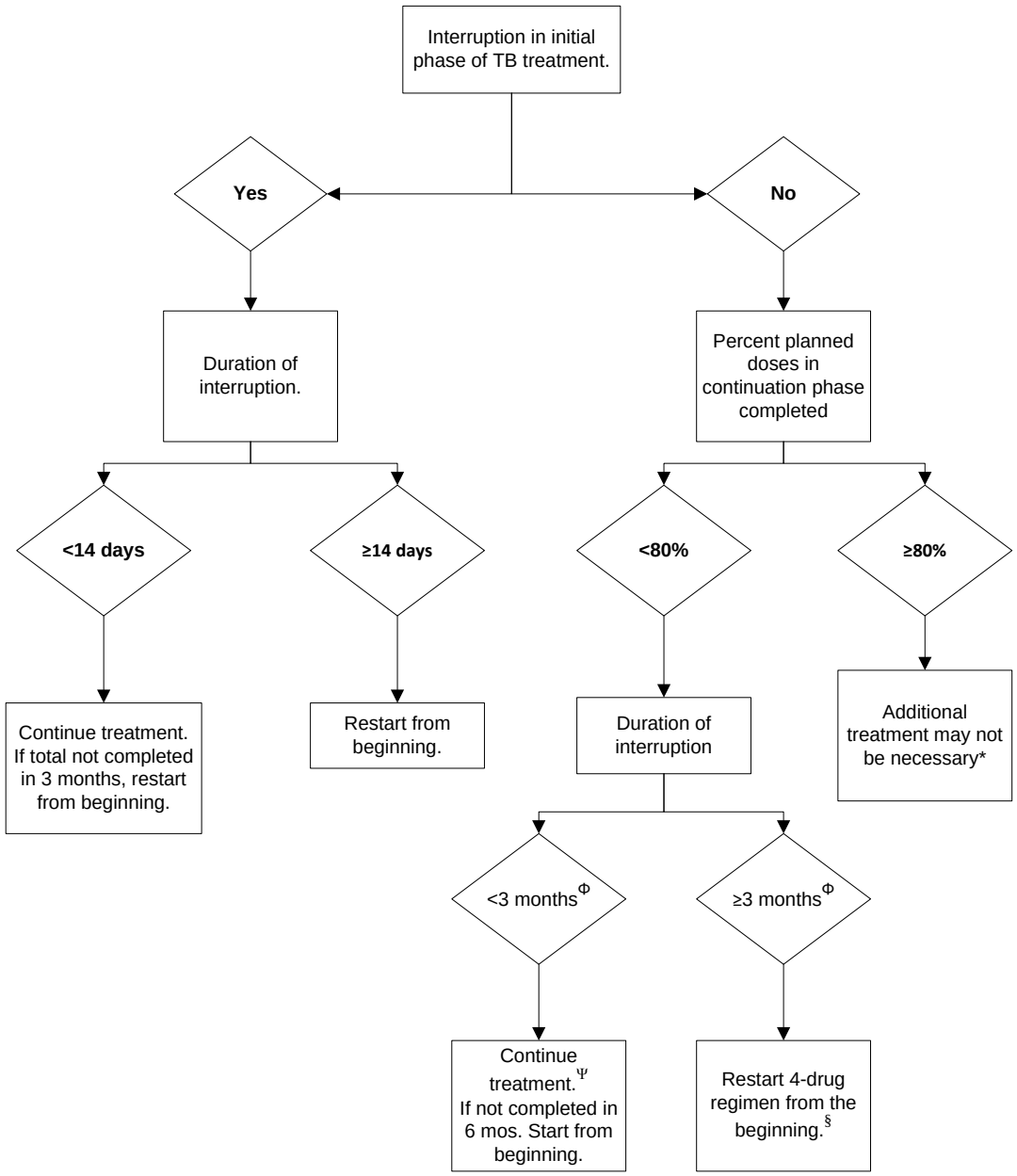
In some cases, either because of drug toxicity or nonadherence to the treatment regimen, the specified number of doses cannot be administered within the targeted period. In such cases, the goal is to deliver the specified number of doses within a recommended maximum time. For example, for a six-month 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 and increased risk for relapse..

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.

See Figure 1: **Management of Treatment Interruptions**[22] for additional information.

Figure 1: MANAGEMENT OF TREATMENT INTERRUPTIONS[23]



* Patients who were initially AFB smear-positive should receive additional therapy.

Φ Recheck smears and cultures and if positive, check drug susceptibility results. Start DOT if not already being used.

Ψ If repeat culture is positive, restart four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, continue therapy to complete regimen within 9 months of original start date.

§ If repeat culture is positive, continue four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, consider stopping therapy if patient has received a total of 9 months of therapy.

Case Closing and End-of-Treatment Evaluation

When patients complete treatment for pulmonary TB, three sputum specimens for AFB and culture, and a chest radiograph should be considered especially for those diagnosed initially with advanced tuberculosis disease. Although a chest radiograph may be difficult and costly for patients living in remote locations, sputa can be collected and mailed to the ASPHL. PHN case managers should also provide their patients with an *End of Treatment Letter* and *Summary* **(18.1)** documenting treatment.

For consultation regarding completion of therapy, end-of-treatment evaluation, or considerations for retreatment, contact the Alaska Tuberculosis Program at 907-269-8000.

Post-Treatment Evaluation

Routine follow-up after completion of therapy is not necessary for patients with *M. tuberculosis* isolates that are susceptible to all first-line anti-tuberculosis drugs and who received a satisfactory and prompt bacteriologic response to a six- or nine-month treatment regimen that included both isoniazid and rifampin. Post-treatment evaluation is also not required for most patients who have *M. tuberculosis* isolates resistant to isoniazid only but susceptible to rifampin, pyrazinamide, and ethambutol and have completed 9 months of treatment with all three of these medications.

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 7: GUIDELINES FOR POST-TREATMENT EVALUATION **

Category of Patient	Frequency of Post-Treatment Evaluation
Drug-susceptible organisms	No reevaluation necessary. Instruct the patient to promptly report the development of any symptoms, particularly prolonged cough, fever, or weight loss. Consider end of treatment evaluation if advanced disease at diagnosis (e.g. 4+ AFB smears and cavitation)
Monoresistance to INH with 6-9 mo. treatment with RIF, PZA, and EMB	No reevaluation necessary. Instruct the patient to promptly report the development of any symptoms, particularly prolonged cough, fever, or weight loss.
INH and RIF resistance	4,8,12,18, and 24 months*
RIF or Rifabutin not used in regimen	4,8,12,18, and 24 months*
Self-administered treatment regimen	4,8, and 12 months*
History of previous treatment, but who have (1) no details available about the treatment, (2) negative sputum cultures, (3) significant changes on CXR, and (4) refuse retreatment	4,8, and 12 months*
No history of previous treatment and who have (1) negative sputum cultures, (2) significant changes on the CXR, and (3) refuse retreatment	4,8, and 12 months*
TB skin test positive and culture negative who are treated empirically because CXR findings are consistent with TB, but who also have other non-TB pulmonary disease.	Refer for further pulmonary evaluation if no response to anti-TB treatment and/or re-evaluate with a CXR every 3-4 months for 1 year.

*Evaluation should include a chest x-ray and the collection of a sputum specimen for smear and culture.

***Adapted from Clinical Policies and Protocols. Bureau of Tuberculosis Control, New York City Department of Health, 4th Edition, March 2008, page p. 116*

For consultation regarding post-treatment evaluation, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

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
- 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
- Advanced age[24]

For consultation regarding treatment in the following situations, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

For detailed information on the treatment of tuberculosis in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 15 years of age) section **9.1**.

For detailed information on the treatment of tuberculosis in special situations, refer to ATS, CDC, IDSA Treatment of Drug-Susceptible Tuberculosis. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .

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.[25]

Drug resistance is proven only by drug-susceptibility testing performed in a competent laboratory. Molecular testing to quickly identify potential resistance to RIF is now available at the Alaska State Public Health 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.[26]

Whenever drug resistance is suspected, please contact the Alaska TB Program at 907-269-8000 to request GeneXpert molecular testing to quickly identify potential RIF resistance.

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.[27]

For consultation regarding the management and treatment of drug-resistant TB, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

Clinical consultation is also available from the Curry International Tuberculosis Center's Warm Line at 877-390-6682.

http://www.currytbcenter.ucsf.edu/consultation

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .
- CDC. "Multidrug-Resistant Tuberculosis" (*TB Elimination Fact Sheet;* accessed January 20, 2017). May 2012. Available at: http://www.cdc.gov/tb/publications/factsheets/drtb/MDRTB.pdf .

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 [28]

Patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations (paradoxical reactions) of TB while receiving antituberculosis treatment.[29]

For consultation regarding the treatment of tuberculosis in HIV-infected patients, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

Clinical consultation is also available from the Curry International Tuberculosis Center's Warm Line at 877-390-6682.

http://www.currytbcenter.ucsf.edu/consultation

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .
- CDC. Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis [online]. 2013. Available at: http://www.cdc.gov/tb/publications/guidelines/TB_HIV_Drugs/PDF/tbhiv.pdf
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 20011). 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*; April 2010). Available at: http://www.cdc.gov/tb/publications/factsheets/treatment/treatmentHIVpositive.pdf
- 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

Persons with TB disease or latent tuberculosis infection (LTBI) who are known or suspected to have an alcohol use disorder or who regularly consume alcohol are at risk for drug-induced liver injury and nonadherence during the course of treatment.

Alcohol consumption increases health risks and can complicate the treatment of tuberculosis and LTBI. Several examples are listed below:

- **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.[30] However, studies have shown that "alcohol consumption is a major risk factor for infection with opportunistic bacterial, viral, fungal, and parasitic pathogens."[31]
- **Liver injury and death**: Drug-induced liver injury "may occur with all currently recommended regimens for the treatment of …LTBI".[32] In the treatment of TB disease, "the crucial efficacy of isoniazid, and particularly rifampin, warrants their use and retention, if at all possible, even in the face of preexisting liver disease."[33] However, it is not fully understood yet how antituberculosis medications cause drug-induced liver injury.[34]

  Persons taking **isoniazid** may have a fourfold greater risk of hepatitis if alcohol is consumed on a daily basis when compared to those who did not drink alcohol.[35] 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.[36,37]

  Pyrazinamide has slightly lower rates of hepatotoxicity than isoniazid or rifampin, but pyrazinamide can cause liver injury that can be severe and prolonged.[38]

  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.[39]

- **Non-adherence 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.[40]

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."[41] 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."[42] DOTS programs that have explicitly offered substance abuse treatment have reported better outcomes that those that have not.[43]

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 and 1991.[44]

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued "An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy." [45] Consult these recommendations at http://www.atsjournals.org/doi/abs/10.1164/rccm.200510-1666ST#readcube-epdf on pages 943-947 for guidance in the following areas for the safe treatment of LTBI and TB Disease:

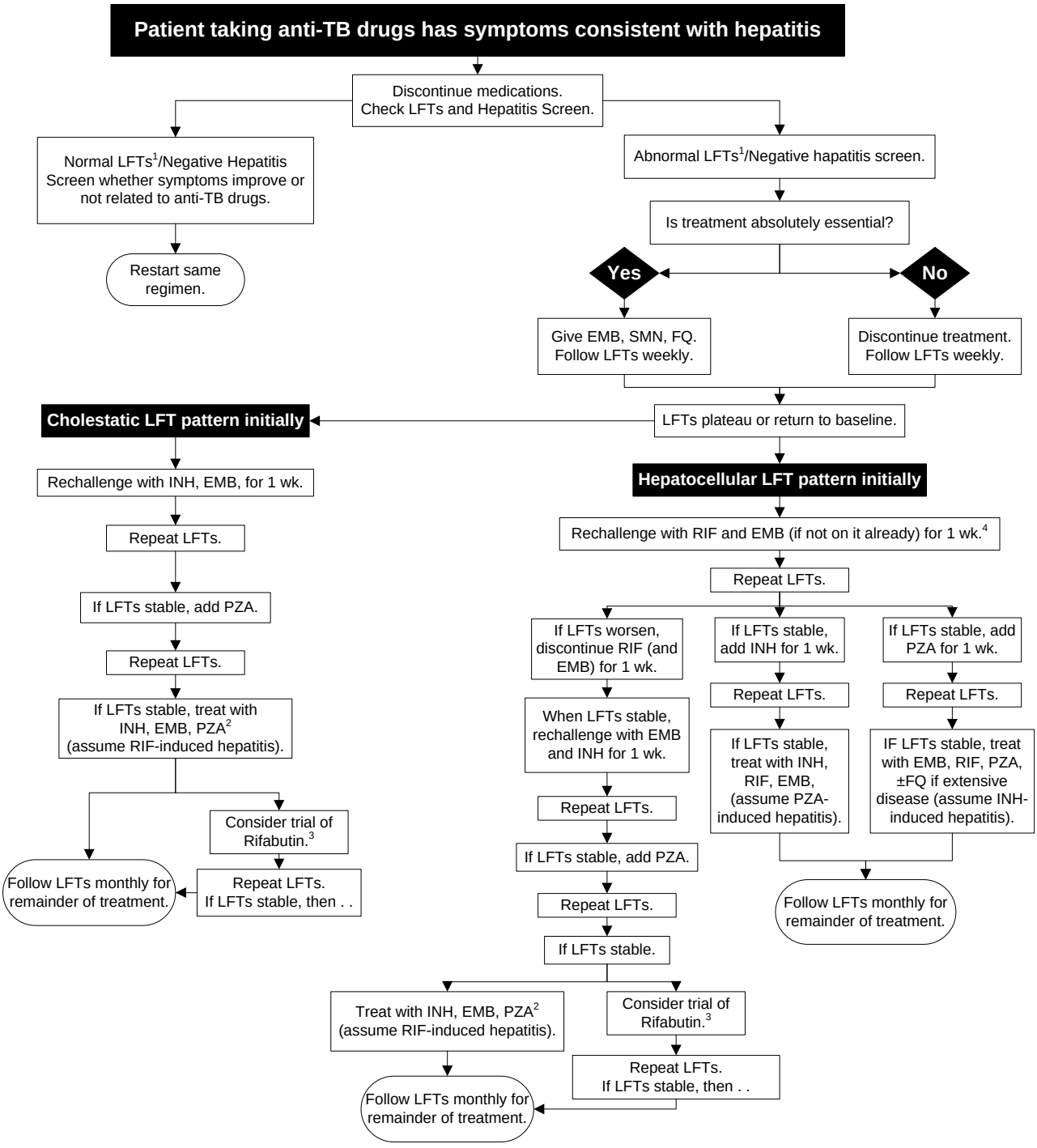
- Program Infrastructure
- Provider Education and Resources
- Pretreatment Clinical Evaluation
- Patient Education
- Medication Administration and Pharmacy
- Treatment of LTBI and Treatment of TB Disease

Restarting Anti-TB Medications in Patients with Drug-induced Hepatitis

For additional information about anti-TB medication reintroduction and monitoring see Figure 3: **Restarting Anti-TB Medications in Patients with Drug-Induced Hepatitis.**

When treating patients with drug induced hepatitis, consultation is available from the Alaska TB Program at 907-269-8000.

Figure 3: RESTARTING ANTI-TB MEDICATIONS IN PATIENTS WITH DRUG-INDUCED HEPATITIS



Abbreviations: EMB-ethambutol; FQ-fluoroquinolone; INH-isoniazid; LFTs-liver function tests; PZA-pyrazinamide; RIF-rifampin; RBT-rifabutin; SMN-streptomycin

1. Abnormal LFTs are ≥3 times the upper limit of normal with symptoms or ≥5 times the upper limit of normal without symptoms.
2. Capreomycin or an appropriate aminoglycoside, and in selected cases a fluoroquinolone, should be considered for the regimen. Treatment needs to last for 18 months unless rifabutin is added successfully. An alternate shorter regimen is isoniazid, streptomycin and pyrazinamide, all given for 9 months.
3. There may be times when rifabutin may be tried in an attempt to decrease duration of treatment from 18 months to 6-9 months.
4. Some clinicians may prefer to challenge with ethambutol and rifampin sequentially rather then simultaneously.

**From Clinical Policies and Protocols. Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, 4rd Edition, March 2008, page p. 109. Found at http://www.nyc.gov/health/tb.*

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. Some patients with underlying liver disease may require treatment with regimens unlikely to cause additional liver injury. Also, fluctuations in the biochemical indicators of liver function (with/without symptoms) related to the preexisting liver disease confound monitoring for drug-induced hepatitis.[46]

For all patients with preexisting liver disease, frequent clinical and laboratory monitoring should be performed to detect drug-induced hepatic injury.[47]

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .

For consultation regarding the treatment of tuberculosis in patients with liver disease, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

Clinical consultation is also available from the Francis J. Curry International Tuberculosis Center's Warm Line at 877-390-6682.

http://www.currytbcenter.ucsf.edu/consultation

Renal Insufficiency and End-Stage Renal Disease

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. To facilitate DOT (three times per week) and avoid premature removal of the drugs, administer all antituberculosis drugs immediately after hemodialysis.[48]

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .

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.[49]

Patients should be screened for risk factors for *M. tuberculosis* infection and tested for infection before initiating immunosuppressive therapies, including TNF-α antagonists. Diagnosis and treatment of LTBI and TB disease should be in accordance with published guidelines.[50]

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.[51]

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

- Initial acid-fast bacilli (AFB) smears, NAA and cultures are negative.
- Clinical or radiographic response occurs within two months of initiation of therapy.
- No other diagnosis has been established.[52]

After the initial phase (first two months), continue treatment with an additional two months of isoniazid and rifampin during the continuation phase to complete a total of four months of treatment.[53] However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of six months.[54]

For consultation regarding the treatment of TB in a patient with negative cultures, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.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.[55] **Exceptions:** For bone or joint TB, use a six- to nine-month regimen.[56] For the meninges, use a 9- to 12-month regimen.[57]
- Consider prolonging therapy for patients with TB in any site that is slow to respond.[58]

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.[59]

For consultation regarding the treatment of extrapulmonary tuberculosis, contact the Alaska Tuberculosis Control Officer at 907-269-8000.

Clinical consultation is also available from the Francis J. Curry International Tuberculosis Center's Warm Line at 877-390-6682.

http://www.currytbcenter.ucsf.edu/consultation

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available

at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .

- Division of Tuberculosis Elimination. *Fact Sheets* (Division of Tuberculosis Elimination Web site; accessed January 2017). 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.[60]

Pyridoxine supplementation (25 mg/day) is recommended for all women taking INH who are either pregnant or breastfeeding.[61]

Resources

- ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf .
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- CDC. Core Curriculum on Tuberculosis (2013) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: http://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.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

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[3] CDC. Chapter 6: Treatment of Tuberculosis Disease. *Core Curriculum on Tuberculosis (2013)* [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter6.pdf . Accessed January 18, 2017.
[4] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.
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[48] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.
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[51] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.
[52] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.
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Diagnosis of Latent Tuberculosis Infection

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska TB Program guidelines to

- classify patients with latent TB infection (LTBI)
- diagnose LTBI

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]

Evaluation and follow-up of contacts are covered in more depth in the Contact Investigation section **11.1**. For information on treatment, refer to the Treatment of Latent Tuberculosis Infection section **8.1**.

For detailed information on the diagnosis and treatment of latent tuberculosis infection in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 16 years of age) section **9.1**.

Policy

In Alaska, TB screening should be provided for:

- Asymptomatic adults with risk factors for LTBI.
- Persons with a greater risk to progress to active TB once infected with *M. tuberculosis* (i.e. those infected with HIV)[2]
- School children, as directed by state regulation. See Statutes and Regulations section **19.6**.
- Persons who are contacts to an active TB case, as described in the Contact Investigation section **11.1**.

For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction **1.18**.

Forms

All required and recommended forms are available in the Forms section of this manual **18.1**.

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[3]

Class	Type	Description
0	▪ No tuberculosis (TB) exposure ▪ Not infected	▪ No history of exposure ▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	▪ TB exposure ▪ No evidence of infection	▪ History of exposure ▪ Negative reaction to the TST or IGRA
2	▪ TB infection ▪ No disease	▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) ▪ No clinical, bacteriologic, or radiographic evidence of TB disease
3	▪ TB disease ▪ Clinically active	▪ *Mycobacterium tuberculosis* complex cultured (if this has been done) ▪ Clinical, bacteriologic, or radiographic evidence of current disease
4	▪ TB disease ▪ Not clinically active	▪ History of episode(s) of TB Or ▪ Abnormal but stable radiographic findings ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (if done) And ▪ No clinical or radiographic evidence of current disease
5	▪ TB suspect	▪ Diagnosis pending

Adapted from: CDC. Chapter 2: Transmission and Pathogenesis of Tuberculosis. *Core Curriculum on Tuberculosis (2013)* [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf . Accessed January 18, 2017.

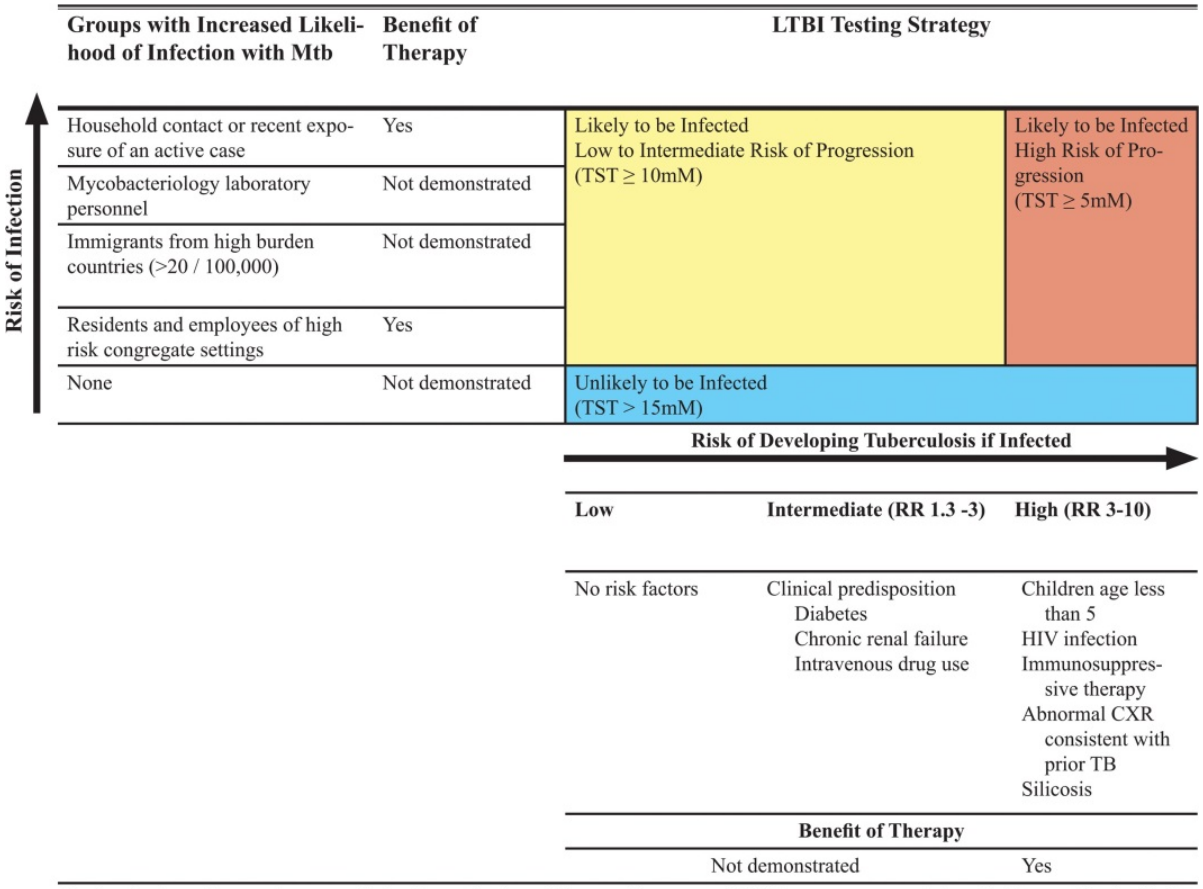
High-Risk Groups

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 3: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease** are candidates for tuberculin skin testing in Alaska.

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 with HIV infection is at much higher risk of having active TB than a US-born individual with HIV infection.

Alaska Natives, especially persons from the Southwest and Northern regions of the state, have an increased likelihood of infection with Mtb.

Figure 1. PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY[4]



In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

Table 3: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE[5,6]

For Tuberculosis Infection	For Progression to Tuberculosis Disease[7]
▪ 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 (<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 here are occurring among immigrants from those countries) ▪ Recent immigrants from Mexico ▪ Migrant workers ▪ Persons who have recently spent over 3 months in high-incidence countries ▪ American Indians/Alaska Natives ▪ Persons with high rates of TB transmission: • Homeless persons • Injection drug users • Persons with human immunodeficiency virus (HIV) infection • Persons living or working in institutions with individuals at risk for TB such as: ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities	▪ 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., leukemias 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.

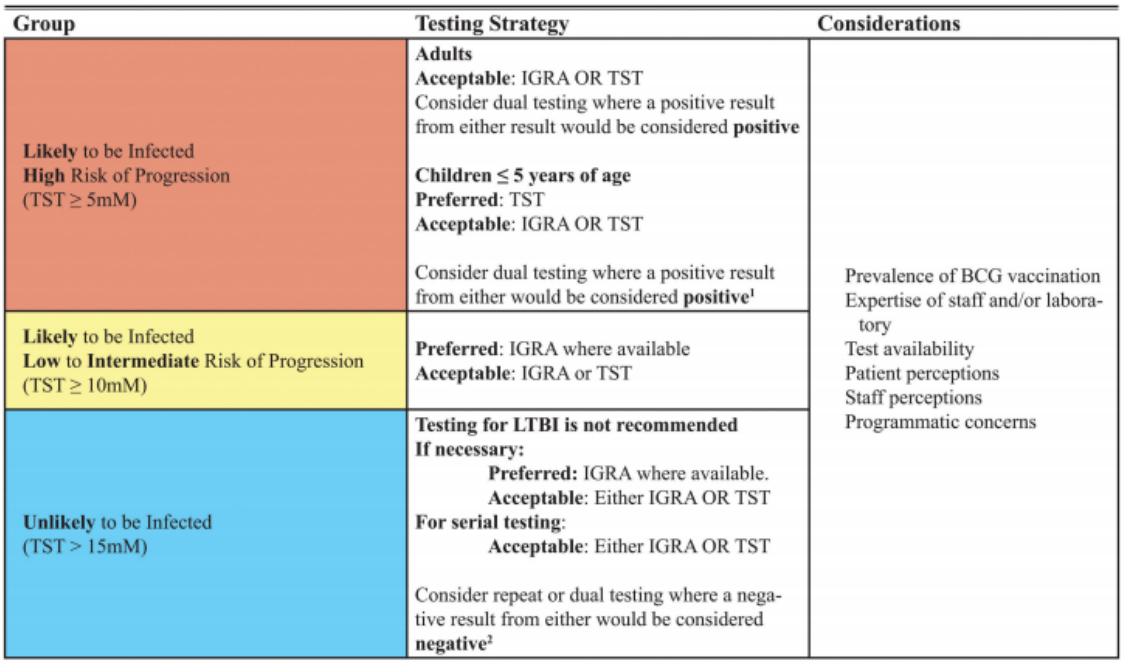
Diagnosis of Latent Tuberculosis Infection

The diagnosis of latent tuberculosis infection (LTBI) has traditionally been based upon results of tuberculin skin testing. However, the QuantiFERON®-TB Gold in-tube (QFT-GIT™) test, a whole-blood interferon gamma release assay (IGRA), is now another option for detecting LTBI.

In December 2016, new *Official American Thoracic Society/ Infectious Diseases Society of America/ Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children* were published. These recommendations suggest performing IGRAs rather than TSTs in all individuals 5 years of age and older who are likely to be infected with Mtb, who have a low or intermediate risk of disease progression and in whom it been decided that testing for LTBI is warranted. A TST is an acceptable alternative, especially where an IGRA is not available, too costly or too burdensome.[8]

Use the Mantoux tuberculin skin test (TST) or an IGRA to test for *Mycobacterium tuberculosis* infection. QFT-GIT™ can be used in all circumstances in which the TST is used, and QFT-GIT™ usually can be used in place of (and not in addition to) the TST. For children under 5 years of age, TST testing is preferred; QFT-GIT™testing is also acceptable for children 2 years and older.

Figure 2. SUMMARY OF RECOMMENDATIONS FOR TESTING FOR LATENT TUBERCULOSIS INFECTION (LTBI)



Group	Testing Strategy	Considerations
Likely to be Infected **High** Risk of Progression (TST ≥ 5mM)	**Adults** **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either result would be considered **positive** **Children ≤ 5 years of age** **Preferred**: TST **Acceptable**: IGRA OR TST Consider dual testing where a positive result from either would be considered **positive**[1]	Prevalence of BCG vaccination Expertise of staff and/or laboratory Test availability Patient perceptions Staff perceptions Programmatic concerns
Likely to be Infected **Low** to **Intermediate** Risk of Progression (TST ≥ 10mM)	**Preferred**: IGRA where available **Acceptable**: IGRA or TST	
Unlikely to be Infected (TST > 15mM)	**Testing for LTBI is not recommended** **If necessary:** **Preferred:** IGRA where available. **Acceptable**: Either IGRA OR TST **For serial testing**: **Acceptable**: Either IGRA OR TST Consider repeat or dual testing where a negative result from either would be considered **negative**[2]	

Figure 2. Summary of recommendations for testing for latent tuberculosis infection (LTBI). [1]Performing a second diagnostic test when the initial test is negative is a strategy to increase sensitivity. This may reduce specificity, but the panel decided that this is an acceptable trade-off in situations in which the consequences of missing LTBI (ie, not treating individuals who may benefit from therapy) exceed the consequences of inappropriate therapy (ie, hepatotoxicity). [2]Performing a confirmatory test following an initial positive result is based upon both the evidence that false-positive results are common among individuals who are unlikely to be infected with Mycobacterium tuberculosis and the committee's presumption that performing a second test on those patients whose initial test was positive will help identify initial false-positive results. Abbreviations: IGRA, interferon-γ release assay; LTBI, latent tuberculosis infection; TST, tuberculin skin test.

Source: ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

Interferon Gamma Release Assays (IGRA) are not provided by or funded by the Alaska TB Program. Reference laboratories currently provide QuantiFERON®-TB Gold in-tube (QFT-GIT™) testing in many communities statewide.

Mantoux Tuberculin Skin Testing

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

In general, it takes 2 to 10 weeks after infection for a person to develop a delayed-type immune response to tuberculin measurable with the Mantoux TST.[9] During the test, tuberculin is injected 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.

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.[10]

Based on the sensitivity and specificity of the purified protein derivative (PPD) TST and the prevalence of TB in different groups, three cut-points are used by CDC for defining a positive tuberculin reaction:

- Greater than or equal to 5 mm
- Greater than or equal to 10 mm
- Greater than or equal to 15 mm of induration[11]

For more information on cut-points for the TST, see the "Interpretation of the Tuberculin Skin Test" topic in this section.

In Alaska, because of our historic and continuing high rates of TB and latent TB infection, any person with a reaction of 10 mm or greater induration is considered TST positive.

Candidates for Mantoux Tuberculin Skin Testing

The Mantoux TST can be administered to all persons, including pregnant women,[12] persons who have previously been vaccinated with Bacille Calmette-Guérin (BCG),[13] 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 **11.1**.

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.

Diagnosis and treatment of LTBI should be considered for BCG-vaccinated persons with a TST reaction of equal to or greater than 10 mm induration, especially if they are

- continually exposed to populations with a high prevalence of TB (e.g., some healthcare workers, employees and volunteers at homeless shelters, and workers at drug treatment centers);
- born or have lived in a country with a high prevalence of TB; or
- exposed to someone with infectious TB, particularly if that person has transmitted TB to others.[14]

[One advantage of the QFT-GIT™ testing if available and affordable is that persons with BCG vaccination will not have a positive QFT-GIT™ test from BCG vaccination.]

Evaluate these patients for symptoms of TB. If a patient has symptoms of TB disease, obtain chest radiography and (if the patient is coughing) collect sputum specimens.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with TST for HIV-infected persons in the U.S.[15]

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that may 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

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.[16] Persons who are symptomatic should receive a chest radiograph and evaluation including sputa collection. Routine chest radiographs are NOT indicated.

Use the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* to document history and TB screening assessment. Forms are available in the Forms section of this manual **18.1.**

See the "Work or school clearance" topic in this section for additional information on clearing individuals with prior positive TSTs for work or school **7.20**.

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.[17] Therefore, if a vaccine containing live virus (for example, measles, MMR, varicella, or live attenuated influenza vaccine) 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 live virus vaccine, one of the following three sequences should be used:

- Apply the TST at same visit as the live virus vaccine.
- Delay the TST at least four weeks if the live virus vaccine is given first
- Apply the TST first and then give the live virus vaccine when the TST is measured[18]

Multiple Puncture Tests

Multiple puncture tests (MPTs), such as the Tine test, should not be used. The MPTs are not reliable because the amount of tuberculin injected intradermally cannot be precisely controlled and there is no standard for interpretation.

Administration of the Tuberculin Skin Test

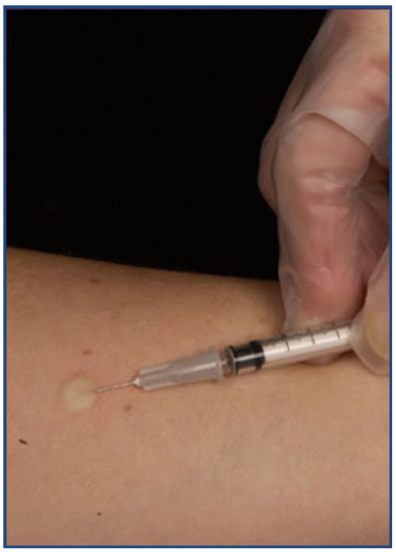
The TST should be placed by a healthcare worker who has received appropriate training and is following written protocols.

Table 4: 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*. Available at: http://www.cdc.gov/tb/education/mantoux/pdf/mantoux.pdf ▪ Your agency's Infection control procedures
Gather Equipment	▪ 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 ▪ Optional: gloves, depending on institutional policy Note: Opened PPD tuberculin vials must be dated and discarded 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 CDC's "Inadvertent Intradermal Administration of Tetanus Toxoid--Containing Vaccines Instead of Tuberculosis Skin Tests" MMWR July 30, 2004 / 53(29);662-664 at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5329a5.htm

How to Administer a Tuberculin Skin Test



If the patient's written consent is required, obtain it, per health department requirements.

1. 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.[19]
2. 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 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. Filled syringes should be kept cool and protected from light. If they are not used within an hour of being drawn up, they should be discarded.
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, name and manufacturer of tuberculin product used, lot number, expiration date, and reason for testing according to clinic or agency protocol.[20]

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.[21]

- A positive reaction can be measured anytime after 48 hours and may be read up to 7 days after placement.
- If the test is read more than 72 hours after placement and the test appears negative, the test should be repeated. It can be repeated immediately, or after one week, if two-step testing is required.

- On a case-by-case basis, TSTs may be read 2-3 hours early or late to avoid not reading them at all. This might occur, for example, when PHNs who itinerate to villages must read a TST when the patient is available or risk having the TST go unread.
- On occasion, TSTs read as negative between 48-72 hours develop measurable induration. If this occurs, call the Alaska TB Program at 907-269-8000 for guidance.

See “Two-Step Tuberculin Skin Testing” in the Infection Control section of this manual **17.11**.

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/pdf/mantoux.pdf .

How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm.
2. Induration is a firm, dense, raised formation. Measure only induration firmness and not swelling around the site of the injection. Do **not** measure erythema (redness). A TST with erythema, but no induration, is 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 and document the result.
4. Report adverse reactions to a TST (e.g., blistering, ulcerations, necrosis) to the FDA’s MedWatch Program at 1-800-332-1088, or via the Internet at http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm

Interpretation of the Tuberculin Skin Test

TSTs should be interpreted by a trained healthcare worker. Use Table 5 below to interpret TSTs.

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/pdf/mantoux.pdf .

For questions or guidance regarding the interpretation of TSTs, call the Alaska TB Program at 907-269-8000.

How to Interpret a Tuberculin Skin Test

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

Table 5: POSITIVE TUBERCULIN SKIN TEST REACTIONS IN ALASKA

Induration Size	Considered Positive For:
5 mm or more	▪ Recent contacts of an infectious case of tuberculosis (TB) disease ▪ Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) ▪ 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	▪ All others in Alaska

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” under “Candidates for Mantoux Tuberculin Skin Testing” in this section **7.9**.

- Recent TB infection (within the past 10 weeks)
- 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” under “Candidates for Mantoux Tuberculin Skin Testing” in this section **7.10**.

- 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:[22]

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

See “Bacille Calmette-Guérin Vaccine” under “Candidates for Mantoux Tuberculin Skin Testing” in this section.

Interferon Gamma Release Assays

TB blood tests are also called interferon-gamma release assays or IGRAs. Two TB blood tests are approved by the U.S. Food and Drug Administration (FDA) and are available in the United States: the QuantiFERON®–TB Gold In-Tube test (QFT-GIT) and the T-SPOT®.TB test (T-Spot).

A health care provider will draw a patient’s blood and send it to a laboratory for analysis and results.

- **Positive TB blood test:** This means that the person has been infected with TB bacteria. Additional tests are needed to determine if the person has latent TB infection or TB disease.
- **Negative TB blood test:** This means that the person’s blood did not react to the test and that latent TB infection or TB disease is not likely.

TB blood tests are the preferred TB test for:

- People who have received the TB vaccine bacille Calmette–Guérin (BCG).
- People who have a difficult time returning for a second appointment to look for a reaction to the TST.[23]

The advantages of IGRA tests, 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.[24] In addition, the IGRA tests are unaffected by past BCG vaccination and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.[25] However, the QFT-GIT test has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. Additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease. [26]

Persons with a positive QFT-GIT result or a positive TST result, regardless of symptoms and signs, should be evaluated for TB disease before LTBI is diagnosed. At minimum, a chest radiograph should be examined for abnormalities consistent with TB disease. [27]

Negative QFT-GIT results 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.[28]

For more information on IGRAs and the QFT-GIT 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

Human Immunodeficiency Virus Screening

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

- Routine HIV screening for all patients ages 13–64 seeking health care for any reason, without regard to patient's known risks for HIV infection
- Annual HIV screening of patients known to be at high risk[29]

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. **(5.8)**. Refer to Table 4: **When to Suspect Pulmonary Tuberculosis in Adults**.

If the person is a contact, follow the procedures for testing and evaluation in the Contact Investigation section **11.1**.

If the person is a participant in two-step screening, see the topic titled "Two-Step Tuberculin Skin Testing" in the Infection Control section **17.11**.

If the TST result is newly positive, a chest radiograph should be obtained for the patient, as specified in the "Chest Radiography" topic in this section **7.17**.

Chest Radiography

All individuals being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease. **Asymptomatic patients whose most recent chest radiograph was taken more than 2 - 3 months prior to starting treatment should have a repeat chest X-ray.** The Alaska TB Program may be able to provide partial reimbursement for patients in need of a chest x-ray but without insurance or financial resources to cover the cost.

Refer to Table 6 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.

PHNs or health care providers should request approval from the Alaska TB Program for partial reimbursement for a single view chest film (CPT 71010) for patients otherwise unable to pay **before** the x-ray is done. Call the Alaska TB Program at 907-269-8000 for an authorization number.

Authorize chest radiographs for patients otherwise unable to pay on the *Request and Authorization for TB Screening and Follow-up Services* **(18.1)** form and send the completed form to the service provider. All chest radiographs requested and authorized should be submitted to the Alaska TB Program for interpretation by our contract radiologist. Comparison films should also be included if available. Please submit all films or digital images and the completed *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** to the Alaska TB Program at 3601 C St, Ste. 540, Anchorage, AK 99503.

Children younger than 5 years of age should receive posterior-anterior and lateral radiographs.[30]

For detailed information on the diagnosis and treatment of latent tuberculosis infection in children, refer to the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 16 years of age) section **9.1**.

For more information on chest radiography, refer to the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians,2nd Edition* (Curry International Tuberculosis Center Web site; 2011) at http://currytbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-04

For persons recently exposed to TB, follow the procedures for testing and evaluation in the Contact Investigation section **11.1**

Chest X-ray Interpretation and Treatment Recommendations

Treatment for LTBI should be prescribed by the patient's health care provider. **For patients without providers or the financial resources to obtain care, the Alaska TB Program recommendations from the Clinical Consultation Summary for LTBI treatment may be used as a prescription for LTBI treatment.** Such patients must be adequately evaluated and have a chest x-ray. The results of the TST or IGRA, review of symptoms, medical history and risk factors should be recorded on the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** and must be submitted to the Alaska TB Program with the chest radiograph for medical review and recommendations.

Table 6: 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 Result?	Recent Exposure to Infectious TB?	Chest Radiograph?	Follow-up Action
Yes	Positive or negative	Yes or no	Normal or abnormal	▪ Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
No	Negative	No	CXR not recommended unless the patient has HIV infection or other forms of immunosuppression are present	▪ No further evaluation or treatment
No	Positive	No	Normal	▪ Treat for LTBI. Refer to the Treatment of Latent Tuberculosis Infection section.
			Abnormal: Noncalcified fibrotic lesions suggestive of old, healed TB; comparison film available and stable	▪ Consider evaluation for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.
			Abnormal: Consistent with TB disease; no comparison film	▪ Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section.

Definitions of abbreviations: CXR = chest radiograph; HIV = human immunodeficiency virus; IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.

Work or School Clearance

Persons with newly positive TSTs or IGRAs may be cleared for work or school if they are low risk by history, asymptomatic and have a negative chest radiograph. Persons with prior positive TSTs may be cleared if they are asymptomatic. Periodic chest radiographs are NOT indicated unless persons with prior positive TSTs or IGRAs are symptomatic for TB.

Use the *Tuberculosis Screening Questionnaire / Chest X-ray Interpretation Request* **(18.1)** to complete history and symptom screening. If history, symptom screening and chest x-ray are negative, the patient may be cleared for work or school by the PHN or provider. Complete the *Tuberculosis Screening and Clearance Card* to document clearance.

*Tuberculosis Screening and Clearance c*ards can be ordered from the Alaska TB Program by calling 907-269-8000.

Resources and References

Resources

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

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Treatment of Latent Tuberculosis Infection

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska TB Program guidelines to

- 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; and
- provide treatment in special situations, such as when a patient is pregnant or is co-infected with both tuberculosis (TB) and human immunodeficiency virus (HIV).

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 infection with *Mycobacterium tuberculosis* organisms (tubercle bacilli), with no symptoms and no radiographic or bacteriologic evidence of TB disease.[2] A person with LTBI is not infectious but can develop active TB disease. **Persons with increased risk for developing TB include those who have recently been infected 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 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 identification and treatment of persons with LTBI at risk for progression to TB.[3]

Healthcare providers must communicate the risks and benefits of treatment to their patients and encourage adherence and treatment completion. Treatment of LTBI is essential to 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]

Detailed information on the diagnosis and treatment of LTBI in children can be found in the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children section **9.1**.

Policy

Treatment should be encouraged for all persons with tuberculosis infection who are determined to be candidates for treatment of LTBI.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

PHNs should provide oversight for all persons taking anti-tuberculosis medications for the treatment of LTBI. This may include: health education; assessing adherence with the prescribed regimen; ordering medications; arranging and monitoring DOT for high risk individuals; assessing for adverse reactions; facilitating evaluation or diagnostic testing; and reporting status and completion of treatment, as needed, to the Alaska TB Program.

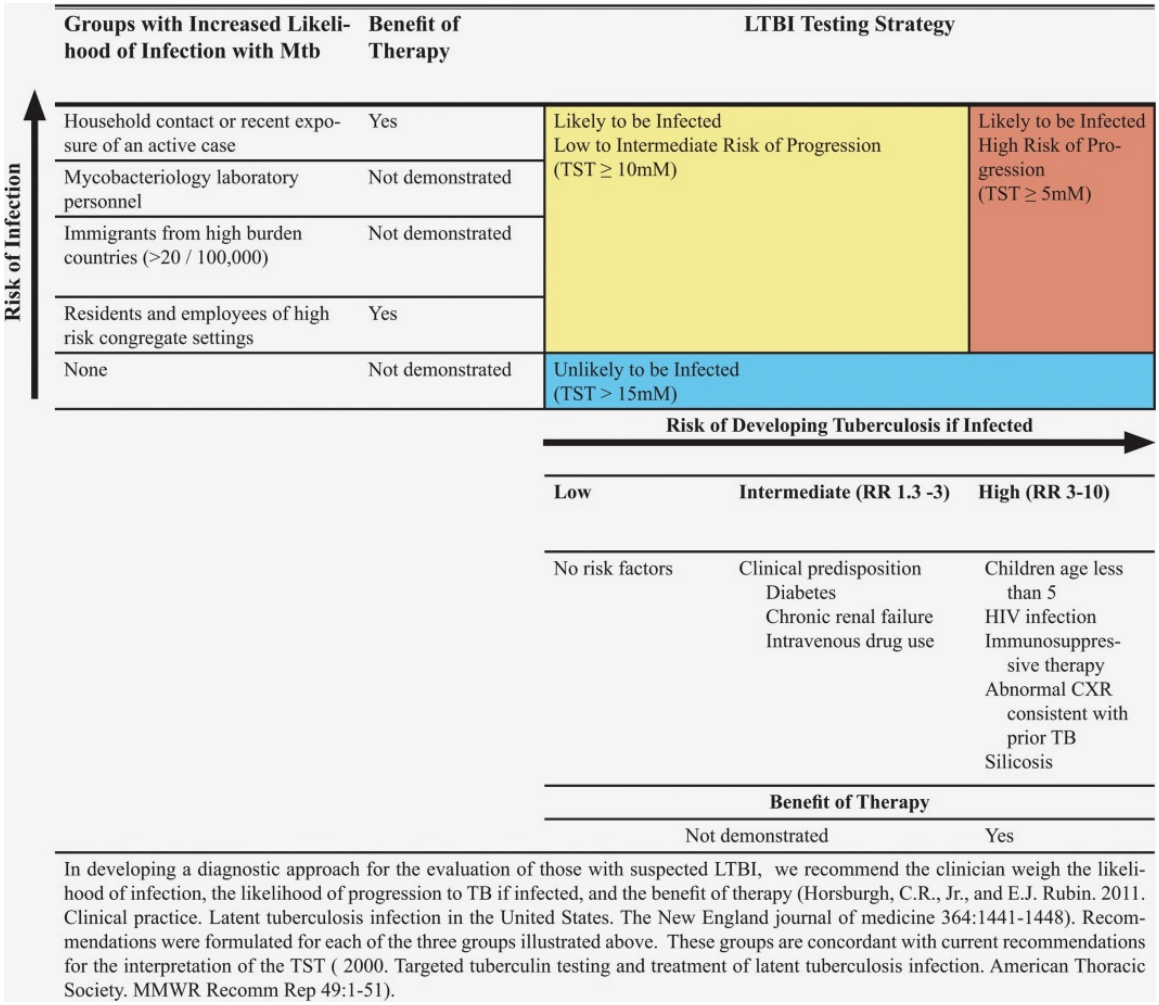
Forms

The *Latent Tuberculosis Infection (LTBI) Treatment Report*, which is used to report LTBI treatment start and completion, is available in the Forms section **18.1**.

Who to Treat

Certain groups are at high risk to develop active tuberculosis (TB) disease once infected, so make every effort to begin appropriate treatment and to ensure those persons complete the entire course of treatment for LTBI.[6]

Figure 1. PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY[7]



Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI regardless of TST results. For more information on time frames, see the "Time Frames for Contact Investigation" topic in the Contact Investigation section **11.12**.

Detailed information on the diagnosis and treatment of LTBI in children can be found in the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children section **9.1**.

Several treatment regimens are available for the treatment of LTBI, and providers should discuss treatment options with their patients.[8] [9]

For consultation regarding the treatment of LTBI, call the Alaska TB Program at 907-269-8000.

Window Period Prophylaxis for 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.[10] 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 had TB disease.[11] Persons who are susceptible and/or vulnerable to TB disease are candidates for **window period treatment.**

Window period prophylaxis is treatment for presumptive TB infection during the interval between infection and detectable skin test or IGRA test reactivity. The National Tuberculosis Controllers Association (NTCA) and the CDC recommend that the window period be estimated at 8 to 10 weeks.[12]

The following contacts with initially negative TST or IGRA 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 at 8 – 10 weeks post exposure 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.

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.[13]

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 consistent with old TB on their chest radiograph
- Persons with organ transplants and other immunosuppressed patients (receiving the equivalent of 15 mg or more/day of prednisone for at least one month)[14]

Tuberculin Skin Test Results of 10 mm or More

In Alaska, all persons with skin test results of 10 mm or more are considered to be positive and should be considered for treatment of LTBI.

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 strongly encouraged to start treatment for their tuberculosis infection.[15]

For a list of high-risk groups, see the "Who to Treat" topic in this section.

High-risk contacts (under 5 years of age or immunocompromised) should be started promptly on treatment for LTBI. For information on time frames, see the "Time Frames for Contact Investigation" topic in the Contact Investigation section. For more information on treatment of LTBI in children, see the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children section **9.1**.

For more information on treatment of LTBI, see the "Treatment Regimens and Dosages" topic in this section and the Centers for Disease Control and Prevention (CDC) publication "TB Elimination Treatment Options for Latent Tuberculosis Infection (LTBI)" (*TB Elimination Fact Sheet; November 2011*) at: http://www.cdc.gov/tb/publications/factsheets/treatment/LTBItreatmentoptions.pdf

Information about the Isoniazid-Rifapentine directly observed regimen is available at:

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

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.

Regimens

Identify an appropriate regimen for the patient using the national guidelines provided in Table 2 below

8.8.

Table 1: LTBI TREATMENT OPTIONS

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)	9 Months	Adult: 5 mg/kg Children: 10-20 mg/kg* Maximum dose: 300 mg	Daily	270
		Adult: 15 mg/kg Children: 20-40 mg/kg* Maximum dose: 900 mg	Twice weekly†	76
	6 months	Adult: 5 mg/kg Children: Not Recommended Maximum Dose: 300 mg	Daily	180
		Adult: 15 mg/kg Children: Not Recommended Maximum dose: 900 mg	Twice weekly†	52
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and Children 12 years of age and over: INH±: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum Children 2-11 years of age: INH 25 mg/kg, rounded to the nearest 50 or 100 mg, 900 mg maximum[16] RPT±: 10.0-14.0 kg 300 mg 14.1-25.0 kg 450 mg 25.1-32.0 kg 600 mg 32.1-49.9 kg 750 mg ≥50.0 kg 900 mg max	Once weekly by DOT†	12
Rifampin (RIF)	4 months	Adult: 10 mg/kg** Children: 10-20 mg/kg Maximum dose: 600 mg	Daily	120

Source: CDC. *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers*. [Division of Tuberculosis Elimination Web site]. Available at: https://www.cdc.gov/tb/publications/ltbi/treatment.htm .

* The American Academy of Pediatric s recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

† Intermittent regimens must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.

±Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until usage.

** In the United States, the recommended regimen for treatment of LTBI in children is a 9-month course of INH. For the treatment of LTBI in infants, children, and adolescents when INH could not be tolerated or the child has had contact with a case patient infected with an isoniazid –resistant but rifamycin-susceptible organism the American Academy of Pediatrics recommends 6 months of daily rifampin (RIF) (180 doses) at a dosage of 10-20mg/kg

The 12-week Isoniazid-Rifapentine regimen

In 2011 the CDC added a new treatment option for LTBI referred to as the 12 dose regimen, a combination of isoniazid (INH) and rifapentine (RPT) given in 12 once-weekly doses by DOT[17]. It is recommended as an alternative to the 9 month daily regimen of INH or rifampin daily for 4 months.

The choice to use INH/RPT depends on eligibility criteria of patients, medical and social circumstances, feasibility of DOT, ability to monitor the patient, and commitment to complete treatment without missing doses.

Table 2: RECOMMENDATIONS AND CONSIDERATIONS FOR USING THE 12-WEEK ISONIAZID-RIFAPENTINE REGIMEN[18]

Consider the regimen for:	Regimen is NOT recommended for:	Comments:
Healthy persons 12 years or older	Children younger than 2 years of age	Therapy may be considered in children ages 2-12 on a case by case basis
Recently exposed contacts of infectious TB and new TB converters	People with HIV/AIDS who are taking antiretroviral treatment	
Persons with radiographic findings of healed pulmonary TB	People presumed to be infected with INH or RIF-resistant *M. tuberculosis*	
HIV infected persons who are not taking antiretroviral medications	Pregnant women or women expecting to become pregnant within the 12–week treatment	
	Individuals who had prior adverse events or hypersensitivity to rifampin	

Source: CDC. Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR 2011; 60(48); 1650-1653.

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/preview/mmwrhtml/mm5231a4.htm

Dosages

The following drugs are available from the Alaska TB Program for treating LTBI. These drugs are provided free of charge upon approval of the TB Program.

- Isoniazid (INH)
- Rifampin (RIF)
- Rifapentine (RPT)

DOT is mandatory for the INH/RPT 12-week regimen. Doses must be administered at least 72 hours apart to be counted.

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. To avoid medication decay, administer as soon as possible after mixing with the food. Possible foods are maple syrup, Nutella, spinach baby food, and chocolate whipped cream. Layer the food and drug on a spoon, and teach the child to take the contents of the spoon without chewing.[19]

For information on ordering drugs, see the Supplies, Materials, and Services section **(16.1).** Additional information can be found in the Case Management section of this manual **10.17.**

For consultation regarding the treatment of LTBI in persons who have been in contact with a case who is resistant to isoniazid and or rifampin, contact the Alaska TB Program at 907-269-8000.

Pyridoxine (Vitamin B6)

Pyridoxine (Vitamin B6) is recommended for some clients taking INH to help prevent peripheral neuropathy. Pyridoxine (vitamin B6) 25-50mg/day is given with INH to all persons at risk of neuropathy, including pregnant women; breastfeeding infants; and persons with HIV, diabetes, alcoholism, malnutrition, advanced age, and or chronic renal failure.[20] For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100mg/d.[21]

Adverse Effects of Drugs Used to Treat LTBI

The patient should be monitored by a public health 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 consulted and the patient monitored more frequently

Some health care providers have concerns about treating patients for LTBI. These concerns are generally related to the length of treatment and the potential side effects of medications. As with any treatment, the health care provider must weigh the risks and benefits for each individual. Obtaining a detailed and accurate medical history, and updating information at frequent intervals, will identify persons who require close monitoring; this will aid the health care provider in determining the most appropriate course of action. In addition, CDC guidelines, drug package inserts, and other authoritative medical sources should be consulted whenever there is a question about side effects or drug-drug interactions.

The sections that follow discuss some of the adverse effects of INH and rifamycins, as well as recommendations for monitoring during treatment and for assessing and ensuring adherence.

Possible adverse effects of INH[22]

- Asymptomatic elevation of serum liver enzyme concentrations occurs in 10%–20% of people taking INH; and liver enzyme concentrations usually return to normal even when treatment is continued. It is generally recommended that INH be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.
- Clinical hepatitis occurs in about 0.1% of people taking INH, and is more common when INH is combined with other hepatotoxic agents. Factors that may increase either of these rates or the severity of hepatitis include daily alcohol consumption, underlying liver disease or risks for liver disease, and the concurrent use of other medications which are metabolized in the liver. Symptomatic hepatitis is rare in patients younger than 20 years of age, but severe and fatal cases have been reported. Younger patients with underlying risk factors for liver disease should be monitored clinically with the same precautions as older patients.
- Peripheral neuropathy occurs in less than 0.2% of people taking INH at conventional doses. It is more likely in the presence of other conditions associated with neuropathy such as diabetes, HIV, renal failure, and alcoholism.

Pyridoxine (vitamin B6) supplementation is recommended only in such conditions or to prevent neuropathy in pregnant or breastfeeding women.

Possible adverse effects of Rifampin (RIF) and Rifapentine (RPT)[23]

- Hepatotoxicity, evidenced by transient asymptomatic hyperbilirubinemia, may occur in 0.6% of persons taking RIF. Hepatitis is more likely when RIF is combined with INH.
- Cutaneous reactions, such as pruritis (with or without a rash), may occur in 6% of persons taking RIF. They are generally self-limited and may not be a true hypersensitivity; continued treatment may be possible.
- Rarely, rifamycins can be associated with hypersensitivity reactions, including hypotension, nephritis or thrombocytopenia, and manifested by symptoms such as fever, headache, dizziness/lightheadedness, musculoskeletal pain, petechiae, and pruritis.
- Gastrointestinal symptoms such as nausea, anorexia, and abdominal pain are rarely severe enough to discontinue treatment.
- Orange discoloration of body fluids is expected and harmless, but patients should be advised beforehand. Soft contact lenses and dentures may be permanently stained.
- RIF and RPT interact with a number of drugs, causing drug-drug interactions. They are known to reduce concentrations of methadone, warfarin, hormonal contraceptives, and phenytoin. Women using hormonal contraceptives should be advised to consider an alternative method of contraception (e.g., a barrier method).
- RIF is contraindicated, or should be used with caution, in HIV-infected individuals being treated with certain antiretroviral medications. Substitution of rifabutin for RIF in the 4-month regimen many be considered for such patients. RPT should not be used in HIV-infected persons taking antiretroviral therapy.

Patient Monitoring and Education During Treatment[24]

To ensure safe and efficacious treatment for LTBI, the health care provider should periodically assess the patient's progress. This evaluation involves clinical monitoring and laboratory testing, as well as patient education.

Clinical Monitoring[25]

- Patients should visit the health care provider who is managing their treatment on a monthly basis to be assessed for the following:
    - Signs of hepatitis
    - Adherence to medication regimen
    - Symptoms of possible adverse drug reactions or interactions
- Patients being treated for LTBI who experience possible adverse reactions should be advised to stop medication and consult their health care provider immediately.

Patient Education[26]

- Explain the disease process and rationale for medication in the absence of symptoms or radiographic abnormalities.
- Review the importance of completing treatment for LTBI.
- Discuss possible side effects of LTBI medications that may include:
    - Fever
    - Unexplained anorexia
    - Dark urine (color of coffee or cola)
    - Icterus
    - Rash
    - Persistent paresthesia of hands and feet
    - Persistent fatigue or weakness lasting 3 or more days
    - Abdominal tenderness, especially in right upper quadrant
    - Easy bruising or bleeding
    - Arthralgia
    - Nausea
    - Vomiting
- Discuss management of common side effects and the need to report to health care provider.

Laboratory Testing[27]

- Baseline laboratory testing (measurements of serum AST, ALT, and bilirubin) is not routinely necessary.
- Laboratory testing at the start of LTBI therapy is recommended for patients with any of the following factors:
    - Liver disorders
    - History of liver disease (e.g., hepatitis B or C, alcoholic hepatitis, or cirrhosis)
    - Regular use of alcohol
    - Risks for chronic liver disease
    - HIV infection
    - Pregnancy or the immediate postpartum period (i.e., within 3 months of delivery)
- Baseline testing can be considered on an individual basis, especially for patients taking other medications for chronic medical conditions.
- After baseline testing, routine periodic retesting is recommended for persons who had abnormal initial results and other persons at risk for hepatic disease.
- At any time during treatment, whether or not baseline tests were done, laboratory testing is recommended for patients who have symptoms suggestive of hepatitis (e.g., fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, dark urine, chills) or who have jaundice. Patients should be instructed, at the start of treatment and at each monthly visit, to stop taking

treatment and to seek medical attention immediately if symptoms of hepatitis develop and not wait until the next clinic visit to stop treatment.

- It is generally recommended that medication be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.

Reporting Reactions

The table below is intended for use by the healthcare worker who performs case management services, such as a public health nurse or a community health aide. The healthcare provider 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 less severe side effect, the healthcare worker should call the patient's provider immediately and monitor the patient.

If a patient reports to a healthcare worker a potentially serious adverse reaction, the healthcare provider should call the patient's provider immediately and alert the Alaska TB Program by calling 1-907-269-8000.

Table 5: REPORTING REACTIONS TO ANTITUBERCULOSIS MEDICATIONS[28]

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 Drug-Susceptible Tuberculosis" (*Clinical Infectious Diseases 2016*; 63[7]:147-95.) at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.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]. November 2011. Available at: . http://www.ctca.org/fileLibrary/file_238.pdf . Accessed January 12, 2017.

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 to the Alaska TB Program by calling 907-269-8000 to report severe adverse events.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 6**: Monitoring and Interventions for Side Effects and Adverse Reactions** to

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

Table 6: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS[29,30,31]

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 In selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy), liver function tests at baseline ▪ aspartate aminotransferase [AST] ▪ alanine aminotransferase [ALT] ▪ serum bilirubin) 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) 25-50mg/day is given with INH to all persons at risk of neuropathy should be considered in clients with: pregnant women, breastfeeding infants, persons with HIV, patients with diabetes, alcoholism, malnutrition, or chronic renal failure, or patients with advanced age.[32] For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100mg/d.[33] 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.

Antituberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (RIF) Rifapentine (RPT) is a rifamycin derivative with a longer half-life. Side-effects and adverse reactions are similar to Rifampin.	▪ Rash ▪ Gastrointestinal upset ▪ Hepatitis ▪ Fever ▪ Bleeding problems ▪ Thrombocytopenia ▪ Renal failure ▪ Flu-like symptoms ▪ Orange-colored body fluids (secretions, urine, tears)	In selected cases ((human immunodeficiency virus [HIV] infection, history of liver disease, alcoholism, and pregnancy), complete blood count, platelets and liver function tests at baseline ▪ aspartate aminotransferase [AST] ▪ alanine aminotransferase [ALT] ▪ serum bilirubin) 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 every month 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 agree and 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 on 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 **13.1**.

Directly Observed Therapy

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

- DOT is mandatory for the RPT/INH 12 week regimen.
- DOT is mandatory for any intermittent regimen.

▪ DOT is strongly encouraged for those with the greatest risk for progressing 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" topic in the Case Management section **10.34**.

For more information on adherence strategies for different developmental stages, see Appendix B 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://globaltb.njms.rutgers.edu/downloads/products/PediatricGuidelines.pdf

Completion of Therapy

Completion of therapy is determined by the total number of doses administered, not on the duration of therapy. When patients have had lapses in therapy but will 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 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 that contacts complete treatment.

All contacts who are being treated for infection should be seen face-to-face by a healthcare provider at least every month or more often. When available, 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 7 describes the duration of therapy and the number of doses that patients are required to take to complete therapy and the time frame within which the total number of doses must be administered for completion of therapy. Please report completion of treatment to the Alaska TB Program.

Table 7: 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 and child	4 months	120	6 months
INH/RPT once weekly	≥ 12 years of age	12 weeks	12	16 weeks
Definitions of abbreviations: INH = isoniazid; RIF = rifampin, RPT= Rifapentine.				

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):26–27; CDC. Regimens. In: Chapter 5: Treatment for Latent Tuberculosis Infection. *Core Curriculum on Tuberculosis: What the Clinician Should Know (2016)* [Division of Tuberculosis Elimination Web site]. Updated May 2016. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter5.pdf . and New England Journal of Medicine. "Three Months of Rifapentine and Isoniazid for Latent TB Infection". 12/8/2011; (vol365)23.p 2155-2165.

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, young children, or persons with human immunodeficiency virus (HIV) for reevaluation.[39]

For consultation regarding completion of therapy and considerations to examine when restarting treatment in noncompliant patients, contact the Alaska TB Control Program at 907-269-8000.

Use the *Latent Tuberculosis Infection* (*LTBI) Treatment Form* to report LTBI treatment Completion. It is available in the Forms section **18.1**.

Treatment in Special Situations

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. Rifampin and rifapentine can adversely interact with many of the antiretroviral HIV medications. Before treatment is initiated, contact the Alaska TB Program at 269-8000 for consultation.

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 the "Time Frames for Contact Investigation" topic in the Contact Investigation section **11.12**.

Resources

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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, 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]

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued "An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy." Available at: http://www.atsjournals.org/doi/full/10.1164/rccm.200510-1666ST#readcube-epdf . Consult these recommendations 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[55] 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.[56]

Pregnancy and Breastfeeding

Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progressing 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. Pregnant women taking INH should receive pyridoxine supplementation.

Women who are pregnant or planning to become pregnant during treatment should not receive the newer INH/RPT regimen. Safety in pregnancy is unknown.

Breastfeeding is not contraindicated when the mother is being treated for LTBI. However, exclusively breastfed infants whose mothers are taking INH should receive supplemental pyridoxine. Note that the amount of INH provided by breast milk is inadequate for treatment of the infant.[57]

Resources and References

Resources

Whom to Treat

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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

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- CDC. Module 4: "Treatment of Tuberculosis and Tuberculosis Infection" (*Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web Site]; 2016). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm

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Adherence

- CDC. Module 6: "Managing Tuberculosis Patients and Improving Adherence" (*Self-Study Modules on Tuberculosis.* Division of Tuberculosis Elimination Web Site; 2016). Available at: https://www.cdc.gov/tb/education/ssmodules/

- 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)

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Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children (under 15 years of age)

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska guidelines to

- detect and diagnose latent tuberculosis infection (LTBI) in children
- detect and diagnose tuberculosis disease in children.
- know when to report suspected or confirmed cases of tuberculosis in children
- follow basic treatment principles for latent tuberculosis infection and tuberculosis disease in children;
- select appropriate pediatric treatment regimens, dosages, and duration;
- monitor pediatric patients for side effects and adverse reactions;
- assess pediatric patients' response to treatment; and
- determine completion of therapy for pediatric patients

Pediatric patients are under 15 years of age.

Children, especially infants and young children under 5 years of age are at increased risk to rapidly develop active and sometimes severe tuberculosis disease after they become infected, because their immune system is immature and not fully developed.

The diagnosis of tuberculosis disease in children, especially in children under 5 years of age, can be difficult because they may have nonspecific signs and symptoms and a small number of mycobacteria. Clinical symptoms, when present, may include fever, growth delay, weight loss or poor weight gain, cough, night sweats, and chills.

Identification of a young child with tuberculosis usually indicates recent transmission from an infectious adult with tuberculosis. It is considered a sentinel event needing urgent and careful investigation.

All children diagnosed with active tuberculosis or LTBI should have a PHN Case Manager assigned.

Call the Alaska TB Program for consultation regarding the evaluation and treatment of pediatric patients with TB and LTBI at 907-269-8000.

For complicated pediatric tuberculosis cases, consult the Curry International Tuberculosis Center Warmline at 877-390- 6682. For more information see http://www.currytbcenter.ucsf.edu/consultation

Report suspected and confirmed cases of pediatric tuberculosis disease to the Alaska Division of Public Health, Section of Epidemiology at 907-269-8000.

Background

Pediatric tuberculosis is defined by the World Health Organization and the US Centers for Disease Control and Prevention as tuberculosis in children less than 15 years of age. Pediatric tuberculosis presents unique challenges. Infants and young children are at increased risk to progress to active disease if infected. Unlike adults and older adolescents who most commonly have reactivation disease, tuberculosis disease in infants and children is usually primary tuberculosis, and this may occur quickly after they become infected. Infants and children have less specific signs and symptoms of disease, some are asymptomatic. The clinical manifestations and radiographic abnormalities seen in children are influenced more by the host inflammatory reaction than by the number of organisms. Administration of tuberculosis medications to infants and children is often difficult. It is also important to remember that pediatric tuberculosis is a sentinel event, reflecting recent transmission from an infectious, often undiagnosed source case in the community.

Pathogenesis of TB

Most children become infected with tuberculosis by inhaling droplet nuclei containing *Mycobacterium tuberculosis (M. tuberculosis)* bacteria that have been expelled by coughing persons with infectious pulmonary or laryngeal TB. Inhaled bacteria are taken up by alveolar macrophages and, if not immediately destroyed, the bacteria cause an initial “primary” pulmonary infection that consists of a small focus in the lung parenchyma that spreads via local lymphatics to regional lymph nodes. When all age groups are taken into account, most tuberculosis infection is asymptomatic and does not result in disease--the primary focus heals, and the bacteria continue to survive in a dormant state that is referred to as latent tuberculosis infection (LTBI). But in infants and young children under five years of age and in children with immune deficiencies, there may be no latent period and the primary infection may progress. There may also be complications related to enlargement of the area of infection in the lung

parenchyma or regional lymph nodes causing wheezing, pneumonia, or atelectasis by compressing or eroding through a bronchus.

Primary tuberculosis infection is usually accompanied by an occult, subclinical bacteremia that seeds distant sites, including the apices of the lungs, the lymph nodes and the central nervous system. In young children and children with immune disorders, severe tuberculosis disease, for example, disseminated (miliary) tuberculosis or TB meningitis, sometimes quickly follows the primary infection, even in the weeks before development of a positive Mantoux tuberculin skin test (TST) or interferon gamma release assay (IGRA). This is the reason why "window period prophylaxis" with isoniazid is recommended for exposed young children and immunocompromised children until infection can be excluded.

The risk of progression to tuberculosis disease following primary infection is mainly related to the age and immune status of the child. The risk is highest in young children under two to three years of age and immunocompromised children.[1] (Table 1). Studies show that disease develops within 1 to 2 years in 40% to 50% of infants with untreated TB infection compared to 15% among older children. Other conditions associated with increased risk of progression include human immunodeficiency virus (HIV) infection; use of immunosuppressive drugs, such as prolonged or high-dose corticosteroid therapy or chemotherapy; intravenous drug use; and certain diseases and medical conditions, for example, Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, and malnutrition. There have been reports of tuberculosis disease in adolescents being treated for arthritis with tumor necrosis factor (TNF) antagonists, such as infliximab and etanercept.

Table 1: AVERAGE AGE-SPECIFIC RISK FOR DISEASE DEVELOPMENT AFTER UNTREATED PRIMARY INFECTION[2]

Age at primary infection	Manifestations of disease	Risk of disease (%)
<1 year	No disease	50
	Pulmonary disease	30-40
	TB meningitis or miliary disease	10-20
1-2 years	No disease	70-80
	Pulmonary disease	10-20
	TB meningitis or miliary disease	2-5
2-5 years	No disease	95
	Pulmonary disease	5
	TB meningitis or miliary disease	0.5
5-10 years	No disease	98
	Pulmonary disease	2
	TB meningitis or miliary disease	<0.5
> 10 years	No disease	80-90
	Pulmonary disease	10-20
	TB meningitis or miliary disease	<0.5

Latent Tuberculosis Infection (LTBI)

Diagnosis of latent tuberculosis infection

Latent tuberculosis infection (LTBI) is defined as M. tuberculosis infection in an asymptomatic person who has a positive Mantoux tuberculin skin test (TST) and / or interferon gamma release assay (IGRA), no physical findings of disease, and chest radiograph findings that are normal or that reveal evidence of healed infection, for example, granulomas or calcifications in the lung, hilar lymph nodes, or both.

The TST and the IGRA are the two methods for diagnosing tuberculosis infection in asymptomatic people.

Current guidelines recommend performing a TST rather than an IGRA in children under 5 years of age. IGRA testing is preferred for children 5 years and older, especially if the child has received BCG vaccination or is felt to be unlikely to return for TST reading, but TST is acceptable, especially if IGRA testing is not available, too costly, or too burdensome.[3]

It is important to remember that children (and adults) with active tuberculosis may have a negative TST or IGRA. This is especially true for infants under six months of age and for infants and children with immune disorders.

Remember: A negative TST or IGRA does not guarantee that a child does not have active tuberculosis.

Candidates for Testing for Tuberculosis Infection

Testing is recommended for children at high risk of tuberculosis infection or progression to tuberculosis disease. Some examples are children who are contacts of a person with active tuberculosis, children with suspected active tuberculosis disease, children with known risk factors for progression of infection to disease, children traveling or residing for 3 months or longer in an area with a high incidence of tuberculosis, and children who arrived in United States from countries with a high tuberculosis incidence within the previous 2 years.

The American Academy of Pediatrics Committee on Infectious Diseases recommends testing of infants, children, and adolescents from several high-risk groups[4]:

Table 2: TUBERCULIN SKIN TEST (TST) AND IGRA RECOMMENDATIONS FOR INFANTS, CHILDREN, AND ADOLESCENTS*

Children for whom immediate TST or IGRA is indicated†
• Contacts of people with confirmed or suspected contagious tuberculosis (contact investigation) • Children with radiographic or clinical findings suggesting tuberculosis disease • Children immigrating from countries with endemic infection (eg, Asia, Middle East, Africa, Latin America, countries of the former Soviet Union), including international adoptees • Children with travel histories to countries with endemic infection and substantial contact with indigenous people from such countries±
Children who should have annual TST or IGRA • Children infected with HIV infection (TST only)
Children at increased risk of progression of LTBI to tuberculosis disease: Children with other medical conditions, including diabetes mellitus, chronic renal failure, malnutrition, congenital or acquired immunodeficiencies, and children receiving tumor necrosis factor (TNF) antagonists deserve special consideration. Without recent exposure, these people are not at increased risk of acquiring *M Tuberculosis* infection. Underlying immune deficiencies associated with these conditions theoretically would enhance the possibility for progression to sever disease. Initial histories of potential exposure to tuberculosis should be included for all of these patients. If these histories or local epidemiological factors suggested a possibility of exposure immediate and periodic TST or IGRA should be considered. A TST or IGRA should be performed before initiation of immunosuppressive therapy, including prolonged systemic corticosteroid administration, organ transplantation, use of TNF-alpha antagonists or blockers, or other immunosuppressive therapy in any child requiring these treatments.

Adapted from Source: American Academy of Pediatrics. [Tuberculosis]. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book®: 2015 Report of the Committee on Infectious Diseases. American Academy of Pediatrics; 2015; XIX

*Bacille Calmette-Guerin immunization is not a contraindication to a TST
†Beginning as early as 3 months of age for TST, 3 Years of age for IGRAs for LTBI and disease
±If the child is well and has no history of exposure, the TST or IGRA should be delayed for up to 10 weeks after return.
Abbreviations: IGRA: indicated interferon-gamma release assay; HIV: human immunodeficiency virus; LTBI: latent *M tuberculosis* infection.

Testing is not recommended for children who are at low risk of tuberculosis infection and disease progression.

Administration and Interpretation of the Tuberculin Skin Test

TSTs should be administered and interpreted by experienced health care professionals who have been trained in the proper methods, because administration and interpretation by unskilled people and family members are unreliable.

The Mantoux method consists of 5 tuberculin units of purified protein derivative (0.1 mL) injected intradermally using a 27-gauge needle and a 1.0-mL syringe into the volar aspect of the forearm. Creation of a visible wheal 6 to 10 mm in diameter is crucial to accurate testing.

The recommended time for assessing the TST result is 48 to 72 hours after administration.

Only the Mantoux TST should be used. Multiple puncture tests are not sufficiently accurate and should not be used.

History of BCG vaccination is not a contraindication to TST.

Detailed information on the administration, measurement and follow-up of tuberculin skin testing can be found in Diagnosis of Latent Tuberculosis Infection Section **7.11**.

A TST can be administered before or at the same time as inactive and live-virus vaccines, including measles-containing vaccine and varicella vaccine. TST has no effect on the response to MMR vaccination. However, measles vaccine (and possibly mumps, rubella, and varicella vaccines) may transiently suppress the TST in a person infected with *M. tuberculosis*. Simultaneously administering TST and live virus vaccine does not interfere with reading the TST at 48 to 72 hours. If the live virus vaccine has already been administered, the TST should be deferred for four to six weeks.[5]

Approximately 10% to 15% of immunocompetent children with culture-documented disease do not react initially to a TST. Host factors, such as young age, poor nutrition, immunosuppression, other viral infections (especially measles, varicella, and influenza), recent tuberculosis infection, and disseminated tuberculosis disease can decrease TST reactivity. Many children and adults co-infected with HIV and *M. tuberculosis* do not react to a TST. Control skin tests to assess cutaneous anergy are not recommended routinely.

Classification of TST results is based on epidemiologic and clinical factors. The size of induration (mm) required for a positive result varies with the person's risk of LTBI and progression to tuberculosis disease.

TABLE 3: POSITIVE TUBERCULIN SKIN TEST REACTIONS IN ALASKA

Induration Size	Considered Positive For:
5 mm or more	▪ Recent contacts of a suspected or known case of tuberculosis (TB) disease ▪ Persons suspected to have tuberculosis disease ▪ Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) ▪ 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	▪ All others

The interpretation of TST results in children who have received BCG vaccination is the same as for persons who have <u>not</u> received BCG vaccine. For more information, see the BCG Section that follows.

The Alaska TB Program recommends prompt clinical and radiographic evaluation of all children and adolescents with positive TST reactions.

Interferon-Gamma Release Assays:

Interferon-gamma release assays (IGRAs) involve incubation of peripheral blood T-lymphocytes with antigens that are specific to *M. tuberculosis*. If an individual has had previous exposure to *M. tuberculosis* his or her T-lymphocytes will respond to the antigens by releasing interferon gamma. Some examples are the QuantiFERON-TB Gold –In Tube (QFT-GIT) test and the T-SPOT.*TB* test. The sensitivity of IGRAs is similar to that of TST for detecting infection in adults with untreated culture-confirmed tuberculosis. One advantage of these tests over the TST is that they are unaffected by BCG vaccination and common non-tuberculous mycobacteria because the antigens used are not found in BCG or most pathogenic nontuberculous mycobacteria.[6] Testing with an IGRA is recommended for children 5 years of age and older who have a history of BCG vaccination or who are unlikely to return for reading of a TST. For other other children 5 years or older, either an IGRA or a TST is acceptable for testing. For infants and children under 5 years of age, testing with a TST is recommended.[7]

As with TSTs, IGRAs cannot distinguish between latent infection and disease, and a negative result from these tests cannot exclude the possibility of tuberculosis infection or disease in a patient with findings that raise suspicion for these conditions.

One advantage of IGRA tests over the TST is that they are unaffected by BCG vaccination and common non-tuberculous mycobacteria. The sensitivity of these blood tests is similar to that of TSTs for detecting infection in adults and children who have untreated culture-confirmed tuberculosis. The specificity of IGRAs is higher than that for TSTs, because the antigens used are not found in BCG or most pathogenic nontuberculous mycobacteria.[8]

IGRAs are recommended by the Centers for Disease Control and Prevention, and some experts prefer IGRAs for use in adults in all circumstances in which a TST is used. The published experience with testing children with IGRAs is less extensive than for adults, but a number of studies have demonstrated that IGRAs perform well in most children 4 years of age and older.[9]

Children with a positive result from an IGRA should be considered infected with *M tuberculosis* complex. A negative IGRA result cannot universally be interpreted as absence of infection. Indeterminate IGRA results do not exclude tuberculosis infection and should not be used to make clinical decisions.[10]

BCG Vaccine

BCG (Bacille Calmette Guérin) vaccine is a live virus vaccine prepared from attenuated strains of *Mycobacterium bovis*. BCG vaccine is widely used in many countries to protect infants and children against severe forms of TB disease including miliary TB and TB meningitis. Use of BCG vaccine is recommended by the Expanded Programme on Immunizations of the World

Health Organization (WHO) for administration at birth and is currently used in more than 160 countries.[11] The on-line BCG World Atlas is a useful resource for determining BCG vaccination policies in over 180 countries.

BCG vaccination has been shown to have relatively high protective efficacy (approximately 80%) against the severe forms of TB disease, meningeal and miliary tuberculosis, in children. The protective efficacy against milder forms of TB disease is less clear; for pulmonary TB the measured efficacy varies significantly, from 0% to 50% in different studies.[12]

BCG is not generally recommended for use in the United States because of the low risk of infection with *M. tuberculosis*, the variable effectiveness of the vaccine against pulmonary TB, and the vaccine's potential interference with tuberculin skin test reactivity.[13]

BCG vaccination can produce a false-positive reaction to the TST. However, most children vaccinated in infancy show no reaction on subsequent TST testing and less than 10% of vaccinated children have a TST reaction ≥10 mm.[14] Children who receive BCG after infancy or those who receive >1 BCG immunization are more likely to have a positive TST.

Children born in countries with high rates of TB disease are likely to have received BCG immunization in infancy, but they are also more likely to have a positive TST from tuberculosis infection than from BCG immunization.[15] The size of the TST after BCG immunization has been shown to correlate with the risk of developing TB disease.

Generally, interpretation of TST results in BCG recipients is the same as for children who have not received the BCG vaccine. A history of vaccination with BCG should not influence the interpretation of the TST reaction or clinical decisions regarding the management of children who are TST positive. Two possible exceptions are when BCG was given within the last 12 months and where the patient is from a low-incidence country.[16]

All children with a positive TST should be promptly evaluated, regardless of BCG immunization status. Tuberculosis disease should be suspected strongly in any symptomatic child with a positive TST result regardless of history of BCG immunization. TST-positive children from countries where TB is common are likely to be infected with TB and are at risk of developing active TB disease, even if they have been vaccinated with BCG.[17]

For children 5 years and older who have received BCG vaccination, testing with an IGRA test is recommended, unless IGRA testing is not available or too costly.

The Alaska TB Program does not provide or pay for IGRA testing at this time.

Management of Children with a Positive IGRA or TST

The most efficient way to prevent pediatric TB is to evaluate and treat those children exposed to an infectious adult source case.

1. ALL infants, children, and adolescents with a positive IGRA or TST should promptly undergo clinical evaluation to rule out active TB disease.

The evaluation should include a history to determine the presence of symptoms of TB disease or coexisting medical conditions that could complicate medical therapy for LTBI or increase the risk of progression to TB disease; a physical examination, and a posterior-anterior (PA) chest radiograph. For children under 5 years of age, a lateral chest x-ray is also recommended.

Latent tuberculosis infection (LTBI) is defined as *M. tuberculosis* infection in a person who has a positive IGRA or TST result, no physical findings of disease, and chest radiograph findings that are normal or reveal evidence of healed infection (for example, granulomas or calcification in the lung, hilar lymph nodes, or both).

2. ALL infants, children, and adolescents who have a positive IGRA or TST result but no evidence of TB disease should promptly receive treatment for latent tuberculosis infection.

Why treat children with latent tuberculosis infection (LTBI)? Children who have LTBI are the reservoir for future tuberculosis disease, hence the importance of LTBI treatment to prevent TB disease and transmission in the future. Treatment of LTBI in children has been demonstrated to provide substantial protection against future development of active TB disease. Prompt treatment is especially important for children under 5 years of age because they are at increased risk of rapid progression to active TB.

Isoniazid given to adults who have LTBI (e.g., no clinical or radiographic abnormalities suggesting tuberculosis disease) provides substantial protection (54%–88%) against development of tuberculosis disease for at least 20 years. Among children, efficacy approaches 100% with appropriate adherence to therapy. All infants, children, and adolescents who have a positive IGRA or TST result but no evidence of tuberculosis disease and who never have received antituberculosis therapy should receive treatment for latent tuberculosis infection.

Treatment of Latent Tuberculosis Infection (LTBI)

Do not start treatment before ruling out tuberculosis disease.

Recommended regimens for treatment of latent tuberculosis infection currently include 1) isoniazid for 9 months, 2) rifampin for 4 months, and 3) for children 2 years and older and adolescents, the combination of isoniazid and rifapentine once weekly by directly observed therapy (DOT) for 12 weeks (3 months.).

Any of these regimens may be used for children without a known source or with a source with a fully susceptible M. tuberculosis isolate. All of these regimens are usually well tolerated by most children.

The shorter regimens –isoniazid and rifapentine once weekly by DOT for 12 weeks and rifampin for 4 months are more expensive but studies find completion rates are higher for short rather than long LTBI treatment regimens.

Rifampin for 4 months would be appropriate for children with LTBI who have been exposed to a source case whose isolate is resistant to INH but susceptible to rifampin or for those who cannot tolerate INH.

Similarly, isoniazid for 9 months would be appropriate children with LTBI who have been exposed to a source case whose isolate is resistant to rifampin but susceptible to isoniazid or for children who cannot tolerate rifampin.

For the isoniazid and rifampin regimens, treatment can be daily or three times per week. Daily treatment can be administered by a parent or caregiver or by DOT. DOT should be used for children on intermittent (3 times per week) treatment. The once weekly isoniazid and rifapentine regimen is always by DOT.

Daily rifampin for 4 months is a suitable alternative for children with LTBI who have been exposed to a source case whose isolate is resistant to INH but susceptible to rifampin or for those who cannot tolerate INH. If daily therapy is not possible, directly observed twice weekly treatment can be used on a case-by-case basis.

The care and treatment of children exposed to a source case with a multidrug-resistant (MDR) *M tuberculosis* strain should be by DOT in consultation with an expert in the management of children with MDR TB.

Before initiating therapy, it is important to educate patients and families regarding signs and symptoms of hepatotoxicity and other side effects and what to do should side effects be noted.

During treatment for LTBI, children should be evaluated at least monthly to reinforce adherence, to be evaluated for toxicities, and to assess possible progression to TB disease.

For consultation regarding the treatment of LTBI, call the Alaska TB Program at 907-269-8000.

Expert consultation with a pediatric TB specialist should be obtained for children judged to be infected with a multidrug-resistant strain of *M. tuberculosis* or HIV. Call the Curry International Tuberculosis Center at 877-390-6682 or visit their website: http://www.currytbcenter.ucsf.edu/consultation

Children who are at especially high risk for TB, and either are suspected of nonadherence or are on an intermittent (for example, three times weekly) dosing regimen, should be treated using DOT. This method of treatment is especially appropriate when a household member is on DOT for TB disease or in institutions and facilities (schools) where a staff member can observe treatment.

LTBI Treatment Regimens and Dosages[18]

The three treatment regimens for latent TB infection (LTBI) use isoniazid (INH) alone, rifampin (RIF) alone, and a combination of isoniazid (INH) and rifapentine (RPT). Treatment must be modified if the patient is a contact of an individual with drug-resistant TB disease. Consultation with a TB expert is advised if the known source of TB infection has drug-resistant TB.

Table 4: LATENT TB INFECTION TREATMENT REGIMENS

Drugs	Duration	Interval	Comments
Isoniazid	9 months	Daily	Preferred treatment for: • Persons with HIV (Rifamycins may adversely interact with many HIV medications.] • Pregnant Women (with pyridoxine/vitamin B6 supplements) • Persons who do not tolerate rifampin therapy
		Three times weekly by DOT	• If daily therapy is not possible, DOT three times a week can be used for 9 months.
Rifampin	4 months	Daily	Rifampin is recommended for persons who are contacts of patients with INH-resistant, RIF-susceptible TB or for persons who do not tolerate isoniazid therapy.
		Three times weekly by DOT	If daily therapy is not possible, DOT three times a week is an option that can be considered on a case-by-case basis.
Isoniazid and Rifapentine	12 weeks (3 months)	Once weekly by DOT	Treatment for: • Current CDC recommendations are to use this regimen for persons 12 years of age and older. On a case-by-case basis, this regimen can be used for persons 2 years of age or older, especially when the likelihood of completing another regimen is low. Not recommended for persons who are: • Younger than 2 years old, • Living with HIV/AIDS taking antiretroviral treatment, • Presumed infected with INH or RIF-resistant M. tuberculosis, and • Women who are pregnant or expect to become pregnant within the 12–week regimen.

Source: Adapted from CDC's Treatment Regiments for Latent TB Infection (LTBI). Available at: https://www.cdc.gov/tb/topic/treatment/ltbi.htm , and AAP Committee on Infectious Diseases 2015 Red Book, personal communication with Dr. Ann Loeffler, Pediatric Tuberculosis Consultant, Curry International Tuberculosis Center.

Dosages

Once the appropriate regimen has been identified, refer to Table 5 for instructions on dosages for each drug. The information in Table 3 is taken from ATS, CDC, and Infectious Diseases Society of America (IDSA) guidelines.

The following drugs are available from the Alaska TB Program for treating LTBI. These drugs are provided free of charge upon approval of the Alaska TB Program.

- Isoniazid (INH)
- Rifampin (RIF)
- Rifapentine (RPT)

Table 5: RECOMMENDED DOSAGES FOR TREATMENT OF LATENT TUBERCULOSIS INFECTION IN CHILDREN

Drug	Preparation	Daily	Three times a Week	Once Weekly Isoniazid + Rifapentine by DOT
Isoniazid (INH)	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml	10–15 mg/kg (Maximum dose 300 mg)[19]	20–30 mg/kg by DOT (Maximum dose 900 mg) [20]	15 mg per kg rounded up to the nearest 50 or 100 mg, by DOT in patients 12 years and older 25 mg/kg rounded to the nearest 50/100 mg in patients 2-11 years[21] (Maximum dose 900 mg)
Rifampin (RIF)	Capsule (150 mg, 300 mg); powder may be suspended for oral administration	10–20 mg/kg Maximum dose 600 mg)	10–20 mg/kg by DOT (Maximum dose 600 mg) [22]	
Rifapentine (RPT)	Tablets (150 mg) Rifapentine tablets can be crushed and administered with semi-solid food for children unable to swallow pills			10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg ≥*50.0 kg* *Maximum dose 900 mg*

Source: Adapted from CDC's Treatment Regiments for Latent TB Infection (LTBI). Available at: https://www.cdc.gov/tb/topic/treatment/ltbi.htm , and AAP Committee on Infectious Diseases 2015 Red Book

All intermittent regimens must be administered by DOT. DOT is the standard of care for all persons diagnosed with tuberculosis in Alaska. It is required for all persons being treated for pulmonary tuberculosis**.**

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 are maple syrup, chocolate syrup, Nutella, spinach baby food, and chocolate whipped cream. Layer the food and drug on a spoon, and teach the child to take the contents of the spoon without chewing.[23]

Monitoring

Children should be seen in the clinic monthly, and questions should be asked about symptoms of toxicity as well as symptoms of active TB, adherence to therapy and results of skin testing of family members and other contacts.

Antituberculosis drug doses should be adjusted in accordance with the weight of the child. Monthly monitoring of body weight is therefore especially important in pediatric cases with adjustment of doses as children gain weight.

Children taking anti-epileptic drugs and either INH or rifampin should be monitored closely because both of these drugs can affect the metabolism and serum levels of anti-epileptics.

Side Effects and Adverse Reactions

Before starting treatment, parents and other caregivers should be taught the possible side effects of the recommended treatment and what to do if their child has any side effects during treatment. Most persons tolerate these medications without problems, but on rare occasion, some persons can have side effects. Routine liver function testing is not indicated for asymptomatic children who do not have underlying liver disease and are not taking other hepatotoxic drugs, although some clinicians recommend checking baseline liver function before starting treatment. Parents and other caregivers should be instructed to stop the medicine immediately and notify us if they note problems, for example

- Loss of appetite, tiredness, weakness, gastric pain, nausea, vomiting
- Numbness or tingling of fingers or toes
- Yellow skin or eyes or dark colored urine
- Fever or chills
- Rashes, hives, bruising, or blistering

Pyridoxine (Vitamin B6):

Routine administration of pyridoxine (vitamin B6) is not recommended for all children taking isoniazid. Pyridoxine supplementation is recommended for:

- exclusively breastfed infants
- children on a milk- and meat-deficient diet,
- children with nutritional deficiencies,
- HIV-infected children,
- pregnant adolescents,
- children who experience paresthesias – numbness, tingling, prickling --while taking isoniazid.[24]

The recommended dose is 6.25 mg (1/4 of a 25 mg tablet) for infants, 12.5 mg (1/2 of a 25 mg tablet) for toddlers, and 25 mg (1 tablet) for school age children. For infants and small children, the tablet portions can be crushed and placed in an agreeable liquid or soft food for administration[25].

Window-Period Prophylaxis

Infants, young children, and children with HIV infection and other immunocompromising conditions are more likely to become ill with tuberculosis disease if they become infected with tuberculosis. They are also more likely to develop severe forms of tuberculosis disease. Because of their increased risk, they are candidates for window-period prophylaxis, which is treatment for presumptive tuberculosis infection during the interval between infection and detectable tuberculin skin test or IGRA reactivity. The National Tuberculosis Controllers Association (NTCA) and the CDC recommend that the window period be estimated at 8 to 10 weeks after last contact with the infectious source case or 8 to 10 weeks after the infectious source case has become non-infectious.[26]

The most efficient way to prevent pediatric TB is to evaluate and treat those children exposed to an infectious adult source case. **ALL** children and adolescents exposed to an infectious case of tuberculosis disease should have a tuberculin skin test or IGRA test and an evaluation for tuberculosis disease. Tuberculin skin testing is recommended for children under 5 years of age. A chest radiograph should be performed on all exposed children under 5 years of age and all exposed children with HIV infection or other immunosuppressive conditions, regardless of their initial tuberculin skin test or IGRA result, to be sure there are no radiographic findings of active tuberculosis before starting window prophylaxis treatment.

Window prophylaxis prevents rapid progression to TB soon after infection. The following contacts with initially negative tuberculin skin test or IGRA results should receive treatment for latent tuberculosis infection (window-period prophylaxis) after tuberculosis 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

For infants over 6 months of age, children and adolescents -- If a second skin test or IGRA test done 8 to 10 weeks after last exposure is negative (TST <5 mm induration or IGRA negative) and the contact doesn't have HIV or another immunosuppressive condition and is no longer exposed to infectious TB, treatment for LTBI (window-period prophylaxis) may be discontinued, and no further follow-up is necessary.

Young infants may be unable to manifest a tuberculin skin test reaction due to their immature immune system. For young infants the Curry International Tuberculosis Center recommends continuing window period prophylaxis until the infant is at least 6 months of age and at least 8 to 10 weeks after last exposure or 8 to 10 weeks after the source case becomes non-infectious before doing the second tuberculin skin test and making a decision whether to continue or stop treatment.[27]

If the second test is negative but the contact is immunocompromised (for example, with human immunodeficiency virus [HIV] infection), a full course of therapy for LTBI should be completed.[28]

Immunocompromised contacts to an infectious TB case, such as HIV-infected contacts, should be given full treatment for LTBI regardless of the TST reaction.[29]

Diagnosis of Tuberculosis Disease

Medical History

The symptoms and signs of pulmonary tuberculosis in children are usually minor and are more common in infants and young children. More than half of infants and children with radiographic evidence of moderate to severe pulmonary tuberculosis have no symptoms or findings and are only discovered by contact tracing. Nonproductive cough and mild dyspnea are the most common symptoms in infants. Fever, night sweats, anorexia, weight loss or poor weight gain, and irritability may also be noted.

It is important to also identify underlying medical conditions, for example HIV infection or other immunosuppressive conditions that increase risk for progression to active TB. Because most children become infected by inhaling droplet nuclei containing *M. tuberculosis* bacteria that have been expelled by coughing persons with infectious pulmonary or laryngeal TB, any possible contacts with adults with confirmed tuberculosis or symptoms of active tuberculosis should be explored.

Physical Examination

Children with primary pulmonary disease often have radiographic abnormalities but are clinically asymptomatic. The chest x-ray findings often have no correlation with signs and symptoms. Physical examination should include an assessment of vital signs including temperature, respiratory rate, and growth parameters. Tachypnea, localized wheezing, or decreased breath sounds can occur with bronchial obstruction, but respiratory distress is rare.

About one-third of children with tuberculosis have extrapulmonary disease. Disease of extrathoracic lymph nodes, especially lymph nodes of the neck (scrofula), is the most common non-pulmonary presentation. Tuberculosis disease can also occur in many other parts of the body, including the pleura, pericardium, meninges, abdomen and gastrointestinal and genitourinary systems, skin, the larynx, and bone and joints.

TABLE 6: SIGNS AND SYMPTOMS OF PULMONARY TB IN CHILDREN[30]

Sign	Infants	Children	Adolescents
Rales	Common	Uncommon	Rare
Wheezing	Common	Uncommon	Uncommon
Fremitus	Rare	Rare	Uncommon
Dullness to percussion	Rare	Rare	Uncommon
Decreased breath sounds	Common	Rare	Uncommon

Symptom	Infants	Children	Adolescents
Fever	Common	Uncommon	Common
Night sweats	Rare	Rare	Uncommon
Cough	Common	Uncommon	Common
Productive cough	Rare	Rare	Common
Hemoptysis	Never	Rare	Rare
Dyspnea	Common	Rare	Rare

Radiology

Chest radiography is an important part of the diagnostic workup of pediatric TB. Because the results may be difficult to interpret, especially if there has been inadequate inspiration or over penetration, films should be reviewed by a radiologist experienced in reading pediatric chest radiographs.

To increase the chances of discerning intrathoracic adenopathy, a common radiographic feature of primary pulmonary TB in children, both posterior-anterior (PA) and lateral chest radiographs are recommended, especially in children under 5 years of age.

A variety of radiographic findings can be seen in children with tuberculosis disease, ranging from normal to diverse abnormalities, such as lymphadenopathy of the hilar, subcarinal, paratracheal, or mediastinal nodes; atelectasis or infiltrate of a segment or lobe; pleural effusion; cavitary lesions; or miliary disease.

With primary disease, lung parenchymal lesions may be anywhere. With reactivation disease, parenchymal lesions are typically but certainly not always in the apical regions.

Table 7. A COMPARISON OF RADIOGRAPHIC FINDINGS NOTED IN ADULT AND PEDIATRIC PATIENTS WITH PULMONARY TB[31]

Characteristic	Adults	Children
Location	Apical	Anywhere (25% multilobar)
Adenopathy	Rare (except HIV)	Usual (30-90%)
Cavitation	Common	Rare (except adolescents)
Signs and symptoms	Consistent	Relative paucity

Radiologic abnormalities in children with active tuberculosis may, in the short term, worsen on treatment before they improve. Usually there has been some response by two months, but even at the end of a satisfactory course of treatment there may be residual lymphadenopathy or scarring.

Magnetic resonance (MR) imaging or computed tomography (CT) imaging for pulmonary tuberculosis is generally not necessary unless there is a questionable abnormality on the plain film and further definition is required. MR and CT imaging may be helpful in the evaluation of suspected active CNS disease, bone and joint disease, pericardium and peritoneum.[32]

Bacteriologic Testing

The gold standard for diagnosing TB disease in children is isolation of *M. tuberculosis* by culture from specimens of gastric aspirates, sputum, bronchial washings, pleural fluid, cerebrospinal fluid (CSF), urine, other body fluids, or a biopsy specimen.

New guidelines recommend collecting and testing respiratory specimens for mycobacterial culture on all children with suspected pulmonary tuberculosis, even when a likely source case has been identified and drug susceptibility results are available for the source case's tuberculosis isolate. Studies have found on occasion the child's *M. tuberculosis* isolate's genotype and drug susceptibility results may differ from those of the identified source case.[33] Collecting respiratory specimens, especially gastric aspirates, from very young children in remote and rural communities across Alaska may very difficult if not impossible due to lack of access to services, logistics and associated travel costs.

In the absence of culture confirmation, diagnosis of active tuberculosis may be made on the basis of a positive tuberculin skin test or IGRA, clinical and radiographic findings suggestive of TB, and history of contact with an identified adult source case. In this case, the drug-susceptibility test results from the source case's *M.tuberculosis* isolate can be used to guide the optimal treatment for the child.

Cultures should always be obtained from the child if the source case is unknown or has a drug-resistant organism and if the child is immunocompromised or has extrapulmonary TB.

Gastric Aspirates

For infants and young children with suspected pulmonary TB, the best specimen to obtain for culture is an early morning gastric aspirate obtained using a naso-gastric tube before the child arises and before peristalsis empties the stomach of the respiratory secretions swallowed overnight. Three consecutive morning gastric aspirates yield *M. tuberculosis* in 40% to 50% of cases; the yield from infants is as high as 90% and up to 77% in symptomatic children with extensive disease.[34]

The Curry International Tuberculosis Center has guidelines for the collection of gastric aspirates, available at http://www.currytbcenter.ucsf.edu/products/pediatric-tuberculosis-online-presentation/resources http://currytbcenter.ucsf.edu/products/product_details.cfm?product

Sputum Collection

For older children collection of spontaneously produced or induced sputum is often possible; nasopharyngeal suctioning can also be used to obtain respiratory specimens. The combination of sputum induction and gastric aspirate has yielded the organism in up to 90% of cases. In older children or adolescents, sputum induction is preferable to bronchoscopy. "Sputum collected from children by nasopharyngeal aspiration or sputum induction with a bronchodilator has a yield of 20%–30%."[35]

Bronchoscopy

The culture yield is lower from bronchoscopy specimens than from properly obtained gastric aspirates. Most children do not need flexible fiberoptic bronchoscopy; but the procedure may be useful in diagnosing endobronchial TB and excluding other causes of pulmonary abnormality, particularly in immunocompromised children, such as those with HIV infection in whom other opportunistic infections may coexist with or mimic TB.

Treatment of Tuberculosis

Basic principles

The goal of treatment is to achieve sterilization of the tuberculous lesions in the shortest possible time. Achievement of this goal minimizes the possibility of development of resistant organisms. The major problem limiting successful treatment is poor adherence to prescribed treatment regimens. Directly observed therapy decreases the rates of relapse, treatment failures, and drug resistance.

Evaluation and treatment of children with TB disease requires a coordinated team approach, including clinicians, public health nurses, and often a social worker and an interpreter. The team should always include a clinician experienced in the management of pediatric tuberculosis. Expert consultation is especially important for any pediatric patient with drug-resistant tuberculosis or co-infected with HIV.

Successful treatment of a child with tuberculosis requires that they swallow each dose of all their medications. All children with tuberculosis disease should be treated by directly observed therapy (DOT). Parents, and in general, family members, should not be relied on to supervise DOT. DOT is the standard of care for all persons diagnosed with tuberculosis in Alaska. It is required for all persons being treated for pulmonary tuberculosis.

The Alaska TB Program at the Section of Epidemiology (907-269-8000) welcomes consultation regarding treatment of pediatric patients with tuberculosis.

TB Consultation For complicated TB cases, for example, children with multi-drug resistant tuberculosis and HIV co-infection, an excellent resource of pediatric TB expertise is the Curry International Tuberculosis Center Warmline Consultation Service 877-390-6682
Weblink: http://www.currytbcenter.ucsf.edu/consultation

Treatment Regimens and Dosages

Regimens

In general, the recommended drug-treatment regimens and duration of treatment for children with tuberculosis are similar to those for adults. Initial treatment should start with daily dosing by DOT, commonly with four drugs for the initial two-month phase and two drugs for the continuation phase of treatment for children with fully susceptible tuberculosis**.**

If the child or the child's source case is known to have a fully-susceptible tuberculosis isolate, it is acceptable to start with a three-drug regimen of isoniazid, rifampin, and pyrazinamide. Otherwise,

ethambutol is always included in the initial treatment regimen until drug susceptibilities are known, to minimize the emergence of drug-resistant strains.

Daily directly observed therapy at least 5 days per week is recommended for both the intensive and continuation phases of treatment. If the child is doing well after completion of the intensive phase of treatment, consideration may be given to changing to thrice weekly treatment, also by DOT, during the continuation phase. Twice weekly treatment is no longer recommended.[36]

The Curry International Tuberculosis Center has a brochure of helpful tips on administration of TB medications to infants and children. These are listed in Appendix A and are available online at: http://currytbcenter.ucsf.edu/pediatric_tb/resources.cfm

Antituberculosis drug doses should be adjusted in accordance with the weight of the child. Monthly monitoring of body weight is therefore especially important in pediatric cases with adjustment of doses as children gain weight.

Duration of Treatment

Drug-susceptible pulmonary disease and hilar adenopathy disease: After treatment for two months with three or four drugs (ethambutol may be discontinued when it becomes known that the child or source case has a fully susceptible *M. tuberculosis* isolate), treatment is continued with isoniazid and rifampin for a minimum of four additional months. The minimum duration of treatment for fully-susceptible pulmonary tuberculosis disease is six months. If the chest radiograph shows a cavitary lesion or lesions and sputum or gastric aspirate specimens remains culture positive after two months of therapy, the duration of therapy should be extended to nine months.

Drug-susceptible extra-pulmonary tuberculosis: Extrapulmonary tuberculosis in children is treated with the same regimens as pulmonary disease, with the exception of CNS tuberculosis, disseminated/miliary tuberculosis, and bone and joint tuberculosis, for which the recommended minimum duration of treatment is nine to twelve months.

Drug-Resistant Tuberculosis or HIV Co-infection: For the treatment of children proven to have or suspected of having drug-resistant TB or HIV co-infection, consultation with a pediatric TB specialist experienced in the management of drug-resistant tuberculosis and TB/HIV coinfection should be obtained. An excellent resource for pediatric TB expertise is the Curry International Tuberculosis Center Warmline Consultation Service 877-390-6682 http://www.currytbcenter.ucsf.edu/consultation

The Curry International Tuberculosis Center and the Tuberculosis Control Branch of the California Department of Public Health have an excellent reference on drug resistant tuberculosis: *Drug-Resistant Tuberculosis: A Survival Guide for Clinicians*, 3rd[d] edition. Available online at http://www.currytbcenter.ucsf.edu/products/view/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition

Table 8: DRUG REGIMENS FOR MICROBIOLOGICALLY CONFIRMED PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS[37]

NOTE: Regimens 3 and 4 are not recommended for pediatric patients

Intensive Phase			Continuation Phase				
Regimen	Drug*	Interval and Dose† (Minimum Duration)	Drugs	Interval and Dose†,±(minimum Duration)	Range of Total Doses	Comments±,**	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182-130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110-94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve	
3	INH RIF PZA EMB	3 times weekly for 24 does (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses††	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior	Lesser

Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

Abbreviations: DOT: directly observer therapy; EMB: ethambutol; HIV: human immunodeficiency virus; INH: isoniazid; PZA: pyrazinamide; RIF: rifampin

* Other combinations may be appropriate in certain circumstance; additional details are provided in the section "recommended Treatment Regimens."

† When DOT is used, drugs may be given 5 days per 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. DOT should be used when drugs are administered <7 days per week.

± Based on expert opinion, patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31-week) continuation phase

** Pyridoxine (vitamin B6), 25-50 mg/day, is given with INH total persons at risk of neuropathy(eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advance age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

†† Alternatively, some US tuberculosis control programs have administered intensive-phase regimens 5 days per week for 15 doses (3 weeks), then twice weekly for 12 doses.

First-Line TB Drugs

The first-line drugs commonly used in the treatment of pediatric tuberculosis, their doses and side effects are summarized in Table 9.

Table 9: COMMONLY USED DRUGS FOR THE TREATMENT OF TUBERCULOSIS IN INFANTS, CHILDREN, AND ADOLESCENTS[38]

Drugs	Dosage Forms	Daily Dosage*, mg/kg	Thrice Weekly Dosage, mg/kg	Adverse Reactions
Isoniazid	Scored tablets 100 mg 300 mg	10–15 (Maximum 300 mg)	20-30 (Maximum 900 mg)	Mild hepatic enzyme elevation, hepatitis, peripheral neuritis, hypersensitivity
Rifampin	Capsules 150 mg 300 mg	10–20 (Maximum 600 mg)	10-20 (Maximum 600 mg)[39]	Orange discoloration of secretions or urine, staining of contact lenses, vomiting, hepatitis, influenza-like reaction, thrombocytopenia, pruritus; oral contraceptives may be ineffective
Pyrazinamide	Scored tablets 500 mg	30-40 (Maximum 2,000 mg)	50 (Maximum 3,000 mg)	Hepatotoxic effects, hyperuricemia, arthralgias, gastrointestinal tract upset
Ethambutol	Tablets 100 mg 400 mg	15–25 (Maximum 1,600 mg)	50 (Maximum 2,400 mg)	Optic neuritis (usually reversible), decreased red-green color discrimination, gastrointestinal tract disturbances, hypersensitivity

Source: ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

* For children unable to receive daily dosing at least 5 days per week, DOT three times weekly can be considered during the continuation phase

Pharmacology and Adverse Reactions

Isoniazid is bactericidal, rapidly absorbed, and well tolerated and penetrates into body fluids, including CSF. Isoniazid is metabolized in the liver and excreted primarily through the kidneys. Hepatotoxic effects are rare in children but can be life threatening.

In children and adolescents given recommended doses, peripheral neuritis or seizures caused by inhibition of pyridoxine metabolism are rare, and most do not need pyridoxine supplements. Pyridoxine is recommended for exclusively breastfed infants and for children and adolescents on meat- and milk-deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children; and pregnant and breastfeeding adolescents and women.[40] For these infants and children, the recommended dose is 6.25 mg (1/4 of a 25 mg tablet) for infants), 12.5 mg (1/2 of a 25 mg tablet)) for toddlers, and 25 mg (1 tablet) for school age children. For infants and small children, the tablet portions can be crushed and placed in an agreeable liquid or soft food for administration[41].

Rifampin is a bactericidal agent that is absorbed rapidly and penetrates into body fluids, including CSF. Rifampin is metabolized by the liver and can alter the pharmacokinetics and

serum concentrations of many other drugs. Hepatotoxic effects, influenza-like symptoms, and pruritus may occur rarely. Rifampin is excreted in bile and urine and can cause orange urine, sweat, and tears and discoloration of soft contact lenses. Rifampin can make oral contraceptives ineffective, so other birth control methods should be adopted when rifampin is administered to sexually active adolescent women.[42]

Pyrazinamide attains therapeutic CSF concentrations, is detectable in macrophages, is administered orally, and is metabolized by the liver. Administration of pyrazinamide with isoniazid and rifampin allows for 6-month regimens in patients with drug-susceptible tuberculosis. Pyrazinamide seldom has hepatotoxic effects and is usually well tolerated by children. Some adolescents and many adults develop arthralgia and hyperuricemia because of inhibition of uric acid excretion. Pyrazinamide must be used with caution in people with underlying liver disease.[43]

Ethambutol is well absorbed after oral administration, diffuses well into tissues, and is excreted in urine. However, concentrations in the cerebrospinal fluid are low. At 15 mg/kg per day, ethambutol is bacteriostatic only, and its primary therapeutic role is to prevent emergence of drug resistance.[44]

A common question is whether the first-line drug ethambutol (EMB) can be safely administered to children. EMB can cause retro bulbar neuritis, a side effect that is dose-dependent and renal-function dependent. It manifests as decreased visual acuity or decreased red-green color discrimination and is usually reversible upon discontinuation of the drug. Monitoring of vision is recommended monthly in older children and adults. Past guidelines have advised against the use of EMB or have advised caution when using EMB in children who cannot verbalize symptoms of optic neuritis, but studies have not found evidence of visual toxicity in young children treated with recommended ethambutol dosing.[45] In young children in whom toxicity cannot be monitored use of EMB in a dose of 15 to 20 mg/kg per day is acceptable and carries a very low risk of optic neuritis.

Monitoring Response to Treatment

Children on TB treatment should be monitored closely for response to treatment and for medication side effects and adverse reactions, especially hepatitis and allergic and non-allergic drug reactions.

Parents and other caregivers should be educated on the TB medications being given to their child and the potential side effects and adverse reactions to watch for and to promptly report if noted while their child is on TB treatment.

A baseline complete blood count with platelet count, chemistry panel with liver function and creatinine, and an HIV screen are recommended for all persons starting treatment for active TB disease.

Medication Side Effects and Adverse Reactions

Follow-up liver function testing should be done at least monthly on children with abnormal baseline liver function and on children co-infected with HIV.

Liver function testing should also be done if a child develops loss of appetite, malaise, abdominal pain, jaundice, or other symptoms of possible hepatitis while on TB treatment.

For children on a TB treatment regimen that includes ethambutol, baseline and monthly follow-up testing of visual acuity and color vision is recommended for children who are able to do these tests, and especially if any vision changes are reported.

Antituberculosis drug doses should be adjusted in accordance with the weight of the child. Monthly monitoring of body weight is therefore especially important in pediatric cases with adjustment of doses as children gain weight.

Children taking anti-epileptic drugs and either INH or rifampin should be monitored closely because both of these drugs can affect the metabolism and serum levels of anti-epileptics.

Pyridoxine (Vitamin B6):

Routine administration of pyridoxine (vitamin B6) is not recommended for all children taking isoniazid. Pyridoxine supplementation is recommended for :

- exclusively breastfed infants
- children on a milk- and meat-deficient diet,
- children with nutritional deficiencies,
- HIV-infected children,
- pregnant adolescents,
- children who experience paresthesias while taking isoniazid.[46]

The recommended dose is 6.25 mg (1/4 of a 25 mg tablet) for infants), 12.5 mg (1/2 of a 25 mg tablet) for toddlers, and 25 mg (1 tablet) for school age children. For infants and small children, the tablet portions can be crushed and placed in an agreeable liquid or soft food for administration[47].

Response to Treatment:

In most children, response to treatment is assessed primarily clinically and by x-ray. In children, weight loss or, more commonly, failure to gain weight adequately is of particular concern as it may be a sign of treatment failure. For children with pulmonary tuberculosis who are able to produce sputum, follow-up sputum cultures at one and three months after starting treatment are recommended, and also if there is a concern of treatment failure. Similarly, follow-up gastric aspirates may be of benefit in infants and young children, especially for those with severe or drug resistant TB disease.

Completion of Treatment

The date of completion of treatment is determined by the total doses administered by DOT and the number of weeks of treatment. If therapy has been interrupted, the date of completion should be extended. Decisions about the completion of treatment should be made in consultation with the Alaska TB Program.

See the Treatment of Tuberculosis section of this manual for more information about determining completion of treatment **6.18**.

Special Issues

Isolation of Children with TB Disease

Most children with tuberculosis disease are not highly infectious. As with older tuberculosis patients, airborne isolation and negative pressure rooms would be appropriate in the hospital setting until testing shows they are not infectious. Airborne precautions with isolation in a negative pressure room are especially important for (1) children with cavitary pulmonary tuberculosis; (2) children with positive sputum AFB smears; (3) children with laryngeal involvement; (4) children with extensive pulmonary infection; or (5) children with congenital tuberculosis undergoing procedures that involve the oropharyngeal airway (e.g., endotracheal intubation); until effective therapy has been initiated, sputum smears demonstrate a diminishing number of organisms, and cough is abating. [48]

The major concern in hospital infection control relates to adult household members and contacts who may be the source case to a child with TB. Household members and other contacts should be managed with tuberculosis precautions when visiting until they are demonstrated not to have infectious tuberculosis. Nonadherent household contacts should be excluded from hospital visitation until their evaluation is complete and tuberculosis disease is excluded or treatment has rendered source cases noninfectious. [49]

Child Care and Schools:

Children with tuberculosis disease can attend school or child care if they are receiving therapy. They can return to school, child care, and regular activities as soon as effective therapy has been instituted, adherence to therapy has been documented, and clinical symptoms have diminished substantially, usually a minimum of 2 weeks after starting treatment.[50]

Source Case Investigations

A diagnosis of latent tuberculosis infection or tuberculosis disease in a young child is a sentinel event representing recent transmission of *M tuberculosis* in the community. Health care providers should assist state and local health department personnel in the search for a source case and others infected by the source case. Members of the household, such as relatives, babysitters, au pairs, boarders, domestic workers, and frequent visitors or other adults, such as child care providers and teachers with whom the child has frequent contact, potentially are source cases.

See the Contact Investigation section of this manual for more information about source case investigations **11.11**.

Drug Delivery Options

Appendix A [51] , by Dr. Ann Loeffler, Pediatric Tuberculosis Consultant, Curry International Tuberculosis Center:

"Drug delivery to children can be very difficult. Prepare the family for the challenge and encourage them not to be discouraged if it takes a week or two to get into a groove. It is better to get the child into a good pattern than to set up a power struggle.

All children with tuberculosis disease (TB) should be treated with directly observed therapy (DOT). With DOT, a health department worker, teacher or other non-family member observes administration of the TB drugs.

Drugs should be taken all at once, not throughout the day, and they should be given close to the same time each day.

Methods to deliver the drugs:

1) Pills and capsules taken intact or in halves: This is the easiest way! Tip the head back to swallow pills and tip the head forward to swallow capsules. If the child can swallow capsules, but not tablets, crush the pills and place the powder in commercially available empty capsules.

2) Pills fragmented (with a knife or commercial pill cutter) or crushed (by commercial pill crusher, mortar and pestle, spoon against spoon or bowl); capsules can be opened.

a) Put a thin layer of soft food onto a spoon. Place the pill fragments or powder on top of the food layer and top with more yummy food. Give the child the dose of medication in this "sandwich." Teach them to swallow it without chewing by practicing without the medication in place first.
   - Chocolate sauce, pudding, fudge sauce, ice cream, etc.
   - Jelly or marmalade (the texture hides the powder granularity)
   - Apple sauce or berry-sauce (better to hide the red rifampin color)
   - Nutella or peanut butter
   - Cream cheese or chili con carne
   - Whatever the family can make work

   The crushed pills have a strong flavor; small fragments of the pill taste better.

OR

b) Suspend in a SMALL AMOUNT of liquid. Water is best. Sugary liquids may interact with INH and should be avoided. Dispense with:
   - Syringe (it is difficult to get the pulverized INH through regular tip syringe other drugs crush finer and solubilize better)
   - Medicine dropper with larger tip; available at many pharmacies
   - Baby bottle (may need to make hole larger)
   - Special Rx MediBottle - with internal sleeve for syringe; available at many pharmacies. Pulverized INH is very difficult to get through this syringe. I suggest giving the other meds with this bottle and then giving INH separately or by the liquid product if it is tolerated by the baby.

- Medicine delivering pacifier; available at many pharmacies (holes will need to be enlarged)

3) Liquids:
   - INH suspension is available commercially in sorbitol. The large osmotic load is poorly tolerated by most children, but may be better tolerated by babies.
   - Other TB medications are not commercially available as liquids. Medications may be suspended by local pharmacies but the stability and homogeneity are not guaranteed.

For more information on delivering TB medications to children consult *Tuberculosis Medication Delivery Tips*, by Dr. Ann Loeffler, Pediatric TB Specialist, Curry International Tuberculosis Center
http://currytbcenter.ucsf.edu/pediatric_tb/resources.cfm

Resources and References

Resources

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Case Management

CONTENTS

Introduction

Purpose

Tuberculosis (TB) case management describes the activities undertaken by the jurisdictional public health agency 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 (case manager) 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 Alaska guidelines to

- 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;
- provide directly observed therapy (DOT);
- use incentives and enablers to improve adherence to therapy; and
- understand when and how to use medical 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.[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 most patients will undergo their initial evaluation and treatment in settings other than a public health agency, a public health agency 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.[9]

Effective TB case management requires administrative commitment and support. This includes education, staff training, and ensuring adequate funding to maintain program activities.[10] It is recognized that local public health agencies differ in their staffing and organization and that no set of guidelines can cover all the situations that may arise relating to case management.[11]

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

In Alaska, regional and local public health nurses (PHNs) function as case managers for each person with suspected or diagnosed active tuberculosis.

All persons suspected or diagnosed with active tuberculosis need a provider or medical home. The case manager should ensure that all patients have a clinical provider to manage their TB treatment and care.

Directly observed therapy (DOT) is the standard of care for all persons diagnosed with tuberculosis in Alaska. It is required for all persons being treated for pulmonary tuberculosis.

PHNs should provide oversight for all persons taking anti-tuberculosis medications for the treatment of LTBI. This may include: health education; assessing adherence with the prescribed regimen; ordering medications; arranging and monitoring DOT for high risk individuals; assessing for adverse reactions; facilitating evaluation or diagnostic testing; and reporting status and completion of treatment, as needed, to the Alaska TB Program.

Forms

Required and recommended forms are available in the Forms section **18.1**.

Consent for Release of Medical Information

Contact Investigation Form

DOT Aide Job Description

DOT Aide Memorandum of Agreement

DOT Calendar

DOT Monthly Invoice for Payment

End of Treatment Letter and Summary

Referral and Authorization for TB Screening and Follow-up Services

TB and LTBI Prescription and Medication Request Form

TB Case Management Form

TB Case Management Information Request

TB Medication Drug Count Worksheet

Tuberculosis Discharge Planning Checklist

Tuberculosis Treatment Contract

Alaska TB Program: Timeline for the Case Management of Tuberculosis Treatment Rev. 1/17

Activity	Weeks 0	1	2	3	4	5	6	7	8	Months 3	4	5	6	9	5	End of treatment evaluation
	Initial Treatment Phase									Continuation Treatment Phase						
Clinical & lab evaluation [1] History & Physical CBC, platelets, creatinine, AST, bilirubin, alk. phosph. Visual acuity, color vision HIV test	X X X X X X				[2] →					→	→	→	→	→		Not recommended
Drugs Refer to CDC. Treatment of Tuberculosis. MMWR 203;52 (No. RR-11)	Isoniazid →									→				→		
	Rifampin →									→				→		
	Pyrazinamide →															
	Ethambutol →									[3]						
Treatment options [4]	All doses should be taken using directly observed therapy (DOT)															
1.) INH, RIF, PZA, EMB	Dose daily (7 days/wk) for 56 doses (8 wks) or 5 days/wk for 40 doses (8 wks). Preferred regimen for patients with newly diagnosed pulmonary TB.									7 days/wk for 126 doses (18 wks) 5 days/wk for 90 doses or twice wkly for 36 doses (18 wks) When appropriate, consider INH + RPT [5]				[6]		Count doses/complete weeks of treatment delivered by DOT to assure treatment completion [7]
2.) INH, RIF, PZA, EMB	Dose daily (7 days/wk) for 56 doses (8 wks) or 5 days/wk for 40 doses (8 wks). Preferred regimen when more frequest DOT during continuation phase is difficult to acheive.									3 days/week for 54 doses (18 wks) [5]				[6]		
3.) INH RIF, PZA, EMB	Dose three times wkly for 24 doses (8 wks.); use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse and acquired drug resistance.									Three times wkly for 54 doses (18 wks)				[6]		
4.) INH, RIF,PZA, EMB	7 days/wk for 14 doses then twice weekly for 12 doses. Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease.If does are missed, thern theraphy can be equivalnet to once wkly, which is inferior.									Twice weekly for 36 doses (18 wks)						
Sputum collection [8]	X				X				X	Collect sputa at least monthly until culture conversion occurs						Optional
Chest x-ray	X									(X)	[9]					Optional
Clinical assessment during treatment [10]	X				X				X	X	X	X	X	X		
DOT & compliance evaluation [11]	X				X				X	X	X	X	X	X		
Contact investigation	Screen priority contacts (TST/IGRA or SX & sputa)								Repeat TSTs/IGRA if initially negative							Confirm completion of contact investigation

[1] If patient has a history of injecting drug use, testing for Heptatitis B and C is recommended.

[2] Repeat liver enzyme tests if signs of drug toxicity appear during treatment. Perform monthly liver enzyme tests if high risk for hepatic toxicity (e.g. pre-existing liver disease or with abnormal liver function that does not require discontinuation).

[3] Discontinue ethambutol if *M. tuberculosis* is sensitive to all first line anti-tuberculosis agents.

[4] INH = isoniazid; RIF = rifampin; PZA = pyrazinamide; EMB = ethambutol; RPT= rifapentine

[5] Regimens listed in order of effectiveness, with 1 being the MOST effective and preferred regimen.

[6] Patients with cavitation on initial CXR and (+) culture at completion of 2 months treatment should receive a 7-month continuation phase.

[7] Consult the Alaska TB program to verify count of DOT doses and determine end of treatment date.

[8] Collect 3 sputa monthly until all 3 are culture negative. Consider more frequent collection if clinically indicated. Repeat susceptibility testing if cultures positive after 3 mos of treatment.

[9] If the patient is culture-negative, a repeat CXR is indicated during treatment to demonstrate improvement. A repeat CXR may also be useful if sputum specimens remains culture positive > 3 mo.

[10] Perform monthly clinical assessments throughout treatment. Ask about nausea, vomiting, abdominal pain or swelling, jaundice, joint pain, vision changes, tingling extremities, or flu-like symptoms. When EMB is part of the regimen, test visual acuity and color vision.

[11] Assess adherence to DOT & treatment plan. Use incentives & enablers. Report ≥ 2 missed DOT doses to the Alaska TB Program.

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, primary care providers, schools, and other healthcare facilities.[12]

When the patient with TB is a child, the case manager should involve both the child and family in the assessment process.[13]

See the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children section for more information **9.1**.

See the "Alaska TB Program: Timeline for the Case Management of TB Treatment" **(10.5)** in this section for more information.

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/products/product_details.cfm?productID=EDP-07 .

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/issues/health-disparities/language-access/language-services-resource-guide-for-health-care-providers

For more information on using interpreters, see the *Addressing Language Barriers* lesson in Module 6: "Managing Patients and Improving Adherence" of the CDC's *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 2013) at https://www.cdc.gov/tb/education/ssmodules/pdfs/module6v2.pdf

Patient's Medical Records

The case manager needs all medical records in order to provide case management and recommend a treatment 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 provider. Without the medical records, the provider may not be able to make the correct judgments in medical management.[14]

Use the *Consent for Release of Information Form* **(18.1)** if necessary to obtain the patient's medical records. Send a copy of the medical records to the Alaska TB Program.

Assessment Site

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.

Due to limited travel schedules, itinerant PHNs may have few opportunities for home visits or in-person visits with patients during their TB treatment. If PHN case managers are having difficulty scheduling face-to-face interactions for initial and follow-up visits with patients, they should consult their Regional Nurse Manager (RNM) or the Alaska TB Program to explore options. Alternatives to home visits or other face-to-face encounters may include teleconferences that include the Community Health Aide/Practitioner

(CHAP), patient, PHN, and the DOT Aide, individual phone calls to the patient, letters, visits by other providers, etc., during the course of treatment.

Whenever possible, start the initial assessment within one business day of the case report for infectious or smear positive pulmonary cases; and within three business days of the case report for others. Itinerants who provide TB case management for patients in remote villages should initiate assessments as soon as possible. See MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis. http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf

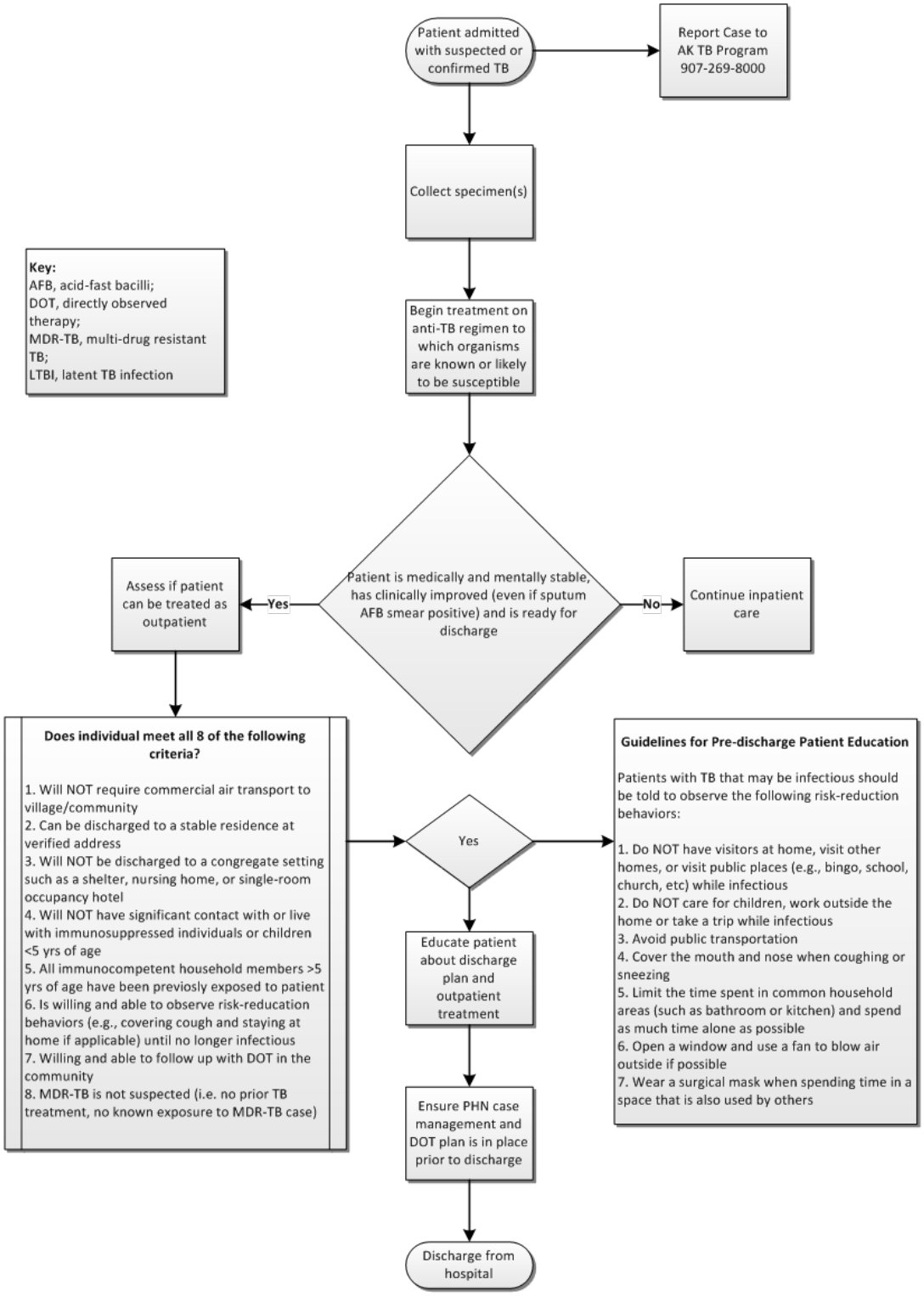
Hospital Discharge Planning

Patients with suspected or diagnosed active TB require collaborative discharge planning before release. 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.[15]

Patients being considered for discharge should meet the following three criteria:

- Complete at least 2 weeks of adequate treatment with anti-TB drugs
- Demonstrate clinical improvement in TB symptoms; and
- Have three (3) consecutive negative AFB sputum smear results collected in 8 – 24 hour intervals (at least one being an early morning specimen).[16]

Figure 1: CRITERIA FOR DISCHARGING PATIENTS WITH SUSPECTED OR CONFIRMED TUBERCULOSIS FROM THE HOSPITAL



Adapted from: New York City Department of Health and Mental Hygiene, Bureau of Tuberculosis Control. Clinical Policies and Protocols, 4th Edition, March 2008.0

Table 1 below provides additional guidance for isolation and release criteria based upon the patient's characteristics at diagnosis.

Table 1: Guidelines for Home and Hospital Isolation of Infectious Tuberculosis Patients

TB Patient Characteristics at Diagnosis	Current Isolation and Release Criteria	Guidelines for Adults and Children with Adult Type Disease*
Sputum Acid Fast Bacilli (AFB) smear positive, and/or NAA positive or patient suspected of having active TB	Hospitalized under inpatient airborne isolation or home isolation and being released to: • General hospitalization, *or* • Outpatient congregate setting, *or* • Home or setting with high-risk contacts	Discharge from airborne isolation patient must meet all the following criteria: 1. Have received standard multidrug anti-TB therapy for at least 2 weeks if original AFB smear positive OR on therapy for 5-7 days if original AFB smear was negative 2. Demonstrated adherence to treatment (DOT) 3. Demonstrated clinical improvement 4. Have 3 consecutive negative AFB smears collected at least 8 hours apart with at least 1 early morning specimen 5. Have no risk factors for drug resistance
Sputum AFB smear negative and TB is not suspected, NAA testing if done is negative and/or another diagnosis is likely	Hospitalized under inpatient airborne isolation and being released to: • General hospitalization • Return to school, *or* • Return to work, *or* • Allowed to travel on commercial/ public transportation	Discharge from airborne isolation patient must meet all the following criteria: 1. Have 3 consecutive negative AFB smears collected at least 8 hours apart with at least 1 early morning specimen 2. TB is not likely and another diagnosis is identified
Sputum AFB smear negative and TB is suspected or confirmed through NAA testing	Hospitalized under inpatient airborne isolation or home isolation and being released to return to normal activities including: • General hospitalization • Return to school, *or* • Return to work, *or* • Allowed to travel on commercial/public transportation	Discharge from home isolation patient *must* meet all the following criteria: 1. Have received standard multidrug anti- TB therapy for at least 5-7 days 2. Demonstrated adherence to treatment (DOT) 3. Demonstrated clinical improvement 4. Have 3 consecutive negative AFB smears collected at least 8 hours apart with at least 1 early morning specimen 5. Have no risk factors for drug resistance

Source: Adapted from Heartland National TB Center. Guidelines for Home and Hospital Isolation of Infectious Tuberculosis Patients. November 2011. Available at: http://www.heartlandntbc.org/assets/products/guidelines_home_hospital_infectious_patients.pdf Accessed January 17, 2017.

Travel

Travel is often a challenging issisue for persons being tretated for tuberculosis in Alaska because of our reliance on air travel. Patients may be medically ready for discharge but may **not** able to travel to their community or village by commercial air or other public transport if they do not have three (3) consecutive negative AFB sputum smear results collected in 8 – 24 hour intervals (at least one being an early morning specimen). This can be an issue for individuals from outlying villages who are hospitalized in Anchorage or other hub communities. The CDC can place the patient on the Do Not Board (DNB) list if it determines that the person 1) is known or believed to be infectious with, or at risk for, serious contagious disease that poses public health threat to others during travel AND 2) not be aware of his or her diagnosis, have been told about the diagnosis and not following public health recommendations, or be unable to be located or 3) be likely to travel on a commercial airplane into, through, or from the US or travel internationally by any means or 4) need to be placed on the DNB and Lookout list to respond to a public health outbreak or to help enforce a public health order. Once a person is placed on the list, airlines are instructed not to issue a boarding pass to the person for any commercial domestic flight or for any commercial international flight arriving in or departing from the United States.[17] Local flying services are not covered by DNB lists and would require a request from the Alaska TB Program to restrict travel for suspected infectious patients until they no longer pose a risk to others. Pilots are responsible for the safety of their flights and may refuse to transport individuals who could jeopardize flight safety. This might include persons who are unruly, intoxicated or masked. Although ferries, trains and busses are not covered by the DNB list, the Alaska TB Program and public health officials would advise against travel for a potentially infectious patient on these conveyances.

Hospital staff should discuss discharge options and plans with the Alaska TB Program to ensure a safe and seamless discharge when the patient is ready. For patients unable to return to their residence because they still have positive AFB smears, the Alaska TB Program may be able to provide assistance for local lodging on a case-by-case basis as the payer of last resort.

Hospitals should notify the Alaska TB Program at least 48 hours (2 business days) before discharging a patient with tuberculosis.

Hospital discharge planners should use the *Tuberculosis Discharge Planning Checklist* **(18.1)** to coordinate discharge planning with the Alaska TB Program and local PHNs. Send a copy of the pertinent medical records to the Alaska TB Program or local PHN, as requested.

Initial Assessment Activities

To complete an initial assessment, perform the following activities:

- Visit the patient's home, hospital room or other location
- If a face-to-face encounter cannot occur, make initial contact with the patient as discussed in the "Assessment Site" topic of this section **10.7**.
- 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 initiate contact investigation
- Evaluate the patient's knowledge and beliefs about TB
- Initiate treatment, if not initiated during hospital stay
- Determine how the supply of TB medications will be ordered and maintained
- Monitor the TB medication regimen
- Identify any barriers or obstacles to adherence
- Review psychosocial status
- Identify and document a good history of the patient's social network
- Gather information for a possible contact investigation
- Consider developing a treatment contract between patient and case manager.

Visit the patient's home. During the patient's TB treatment, at least one or more home visits should be conducted, if possible. 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 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).[18] 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.

Due to limited travel schedules, itinerant PHNs may have few opportunities for home visits or in-person visits with patients during their TB treatment. If PHN case managers are having difficulty scheduling face-to-face interactions for initial and follow-up visits with patients, they should consult their Regional Nurse Manager (RNM) or the Alaska TB Program to explore options. Alternatives to home visits or other face-to-face encounters may include individual phone calls to the patient, teleconferences that include the

Community Health Aide/Practitioner (CHAP), patient, PHN, and the DOT Aide, letters, visits by other providers, etc., during the course of treatment.

Obtain or review demographic information, including the name, address, telephone number(s), birth date, and health insurance provider's name, address, and identifying information.[19]

Ascertain the extent of TB illness, including acuity and length of symptoms, bacteriology and radiographic findings, laboratory analyses, tuberculin skin test results, nutritional status, vital signs, and baseline weight (without shoes or excess clothing).

The responsible health care provider and the Alaska TB Program should be consulted immediately upon receipt of a case of suspected tuberculosis. Within one week of a case report, a tuberculin skin test should be placed, measured, and interpreted; 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 Alaska State Public Health Laboratory. The PHN may also collect sputa, arrange for a chest radiograph, and facilitate a provider evaluation and baseline laboratory testing as needed.

Use the *Referral and Authorization for TB Screening and Follow-up Services* **(18.1)** to refer uninsured patients for a single view chest radiograph or hepatic panel/liver function tests if necessary. The Alaska TB Program will provide partial reimbursement for services as indicated on the form. See the "Chest Radiography" topic in the Diagnosis of LTBI section **(7.17)** of this manual in for more information.

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.[20] Adults who are suspected of TB or who are active cases usually need only an initial posterior-anterior chest radiograph.

See the Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children section for more information **9.1**.

See the "Alaska TB Program: Timeline for the Case Management of TB Treatment" **(10.5)** in this section for more information.

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, allergies, or medications that may interfere with TB drugs. The case manager should obtain the names, addresses, and telephone numbers of the patient's primary care 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 (MDR-TB) and extremely drug resistant (XDR-TB).). It is also important to determine what the patient perceives as his or her most important medical/health problem. The date of the last menstrual period and contraceptive use should be obtained from female patients.[21]

Some antituberculosis medications may interfere with hormonal contraceptives. For more information, see the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section **6.13**.

Determine infectiousness or potential infectiousness and initiate contact investigation. To determine where and on whom to initiate contact investigation, the initial assessment should gather information to define the start and end dates of the period of infectiousness. 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. The parameters of a contact investigation, including the need for repeating the tuberculin skin test for contacts that were initially negative, can then be determined.[22]

For more information on the period of infectiousness and when to initiate contact investigations, see the Contact Investigation section **11.1**.

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.[23]

Initiate treatment. 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 (military) 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 ATS, CDC, IDSA's *Diagnosis of Tuberculosis in Adults and Children* (2017) at https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf).

Directly observed therapy (DOT) is the standard of care for all persons diagnosed with pulmonary tuberculosis in Alaska. It is also recommended for all persons diagnosed with extrapulmonary tuberculosis.

Determine how the supply of TB medications will be ordered and maintained. The PHN case manager should order drugs immediately upon receipt of medical orders which document drugs, dose, route, frequency, and duration.

Information on ordering TB medications is discussed in the "Ordering Medications for the Treatment of Tuberculosis" topic in this section **10.18**.

It is the responsibility of the prescribing provider to ensure that newly-prescribed anti-tuberculosis medications do not interact unfavorably with prescription or over the counter medications that the patient is currently taking. Additional information on common drug interactions can be found in the "Monitoring for Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis section of this manual **6.15.**

Monitor the TB medication regimen. The case manager should ensure that medications and dosages are prescribed according to current American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines. 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 the right doses and observe patients swallow medications. Tuberculosis medications should be given once daily, both inpatient and outpatient. The patient's tolerance to TB medications should be noted, and interactions with other medications should be determined prior to the patient starting TB medications.[24]

For more information on treatment regimens and dosages, see the Treatment of Tuberculosis Disease section **6.6**.

Identify any barriers or obstacles to adherence in taking TB medications and keeping provider 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.

It is very important for case managers to identify, document, and report nonadherence with TB treatment and DOT to the Alaska TB Program as soon as possible. If DOT Aides are observing patients taking TB medications, they should also be instructed to report two (2) or more consecutive missed DOT doses to the PHN case manager as soon as possible.

Review psychosocial status to identify unmet needs, the use of alcohol and/or illegal drugs, and any pre-existing psychiatric diagnoses.[25]

Identify and document a good 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, bingo, circuit parties, faith-based functions, and other venues.

For more information see the Contact Investigation section of this manual **11.1**.

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.

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** because it tailors treatment to the 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.[26]

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.[27]

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.[28] The treatment plan should be reviewed and updated as needed during reviews of clinical progress.[29]

The Alaska TB Program conducts monthly TB case management meetings or teleconferences with PHNs and providers in several regions of the state. Individual patient status and treatment plans are discussed and recommendations provided during these meetings.

See the "Alaska TB Program: Timeline for the Case Management of TB Treatment" **(10.5)** in this section for more information.

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 workers, other caregivers (outreach workers, nurses), and person managing the contact investigation
- Method for prevention of transmission: no isolation, airborne infection isolation, home isolation, legal order for isolation
- *Tuberculosis Treatment Contract* signatures of the PHN case manager and the patient (or patient's representative), if a treatment agreement is used
- 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
- Means of ensuring successful completion of treatment (DOT, incentives, enablers)
- Location(s) where DOT will be administered[30]

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. [31] DOT is the standard of care for all TB cases and suspects.

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 health care provider's office. When itinerant PHNs provide case management for patients in villages, monthly monitoring can be done by teleconference in conjunction with the CHAP or DOT Aide, phone, or may be done by the patients' provider. 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.[32]

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.[33]

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
- Broker and locate needed services relating to TB treatment
- Negotiate a plan for DOT
- Coordinate strategies to improve adherence

Refer the patient to other healthcare providers, social service agencies, or community organizations, as needed. All patients being treated for active tuberculosis need a medical home. 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.[34] All patients with suspected or proven TB should be tested for HIV, 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 each referral to obtain medical information and to determine whether the necessary medical intervention has been completed.

Locate needed services relating to the TB treatment. This may include laboratory, auditory, or visual acuity testing; additional radiographs; or other tests required specifically for the patient. Schedule or assist the patient in scheduling appointments and 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. Lack of financial resources or health insurance will affect the patient's willingness to keep appointments, which may be critical to his or her health. The case manager may need to discuss essential services with insurance companies or other healthcare providers to obtain the most cost-effective, quality service.[35] Help the patient access financial assistance and receive treatment for psychosocial, alcohol-related, and drug-related conditions.

Negotiate a plan for DOT. DOT should be the standard of care for all patients. The case manager should ensure the plan is suitable for the patient's needs and may consider having the patient sign a treatment 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 outside organizations, such as school nurses or drug treatment center nurses.[36]

Refer to the "Directly Observed Therapy" topic in this section **10.32**.

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. A written contract detailing the agreed upon responsibilities of both the patient and the case manager may be useful to improve adherence to treatment. When incentives and enablers are used, they should be meaningful and specific for a particular patient.[37] Incentives and enablers may be considered for use with all patients.

Use the *Tuberculosis Treatment Contract* to document the responsibilities of the patient and PHN case manager. It is available in the Forms section of the manual **(18.1).**

The Alaska TB Program has limited funding resources for incentives and enablers. Persons being treated for active tuberculosis are the **priority** for incentives and enablers. PHN case managers should apply for funds through their Regional Nurse Managers.

Ordering Medications for the Treatment of TB

The Alaska TB Program provides medications for the treatment of tuberculosis and LTBI free of charge. The PHN case manager should order drugs immediately upon receipt of medical orders. The new *TB/LTBI Prescription and Medication Request* **(18.1)** can be used as a prescription by the provider and may also be used by the PHN case manager to order medications for patients. When providers do not use the new form as a prescription, please include a copy of the prescription with the initial medication request. Antituberculosis medications can be sent directly to the PHN case manager, a clinic or licensed provider.

All providers prescribing and /or requesting medications from the SOE Drug Room agree to use standard and approved regimens as referenced in this AK TB Manual to treat individuals for suspected or confirmed tuberculosis or LTBI. In special situations and after consultation with the Alaska TB Program, other regimens may be approved if clinically indicated.

- Requests for TB medications should be faxed to the Alaska TB Program at 907-563-7868. Please allow at least 2 weeks for processing and shipping. A hardcopy of the drug order DOES NOT need to be mailed.
- The medication order should state the name of the drug(s), dose, route, frequency, and number of doses.
    - Request the total number of DOSES required to complete therapy for each medication.
    - Indicate the number of doses provided from stock or another source – e.g. hospital pharmacy at discharge.
- Most medications are available in unit dose packaging or in bottles. All DOT medications are supplied in labeled unit dose packs. **Dose packs are NOT child proof and must be stored safely and out of the reach of children at all times**. The SOE Drug Room can assist with safe storage options for DOT Aides if requested by PHNs.
- The SOE Drug Room can compound orders and assist with special dosing. Pill splitters, crushers and liquid measuring devices are available.

- Monthly auto refills are generated by the SOE Drug Room. Each week, the Epi Drug Room will notify PHNs of medication refills for the week. The PHN should review and inform the pharmacy of any changes in therapy – discontinued medications, dosage or regimen changes, treatment interruptions, etc.
- Second line and special order drugs – Amikacin, Streptomycin, etc. – must be special ordered and are NOT available by auto refill.
- Drug monographs (patient information sheets) are automatically included with each new prescription. Please specify if you need a language other than English. These must be provided to the patient for each new TB medication.

All discontinued, unused or close-dated medication should be returned to the SOE Drug Room as soon as possible. Mail all returns to: SOE Drug Room, 9210 Vanguard Drive, Suite 102A, Anchorage, AK 99507

Use the *TB/LTBI Prescription and Medication Request* to order TB medications for a specific patient. Stock supplies can be ordered using the *TB/LTBI Stock Medication Request*. When returning unused or close-dated medications, use the *TB/LTBI Medication Return Form.* Forms are available in the Forms section of the manual **18.1**.

The TB/LTBI Prescription and Medication Request Guidelines contain detailed information on ordering and storing antituberculosis medications. It is available in the Forms section of the manual **18.1**.

Ongoing Assessment and Monitoring

Conduct ongoing assessments and monitor patients at least **monthly** either in an ambulatory clinic setting, local public health agency, or private physician's office. When itinerant PHNs provide case management for patients in villages, monthly monitoring can be done by teleconference in conjunction with the CHAP or DOT Aide, by phone with the patient, or may be done by the patients' provider. 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) or follow-up appointments.[38]

There are countless stories from nurses and outreach workers reinforcing the fact that not all information is obtained from the patient or family at one time. Therefore, the case manager must ensure that the list of contacts is updated from time to time and determine the need for further testing. It is also important to review the status of the contact investigation to ensure that timelines and standards are followed. Also, checking for the accuracy of previously gathered information should occur throughout the patient's TB treatment.[39]

See the "Alaska TB Program: Timeline for the Case Management of TB Treatment" **(10.5)** in this section for more information.

Ongoing Assessment Activities

To complete an ongoing assessment, perform the following activities:

- Monitor the clinical response to treatment
- Determine human immunodeficiency virus (HIV) status and the risk factors for HIV disease, and refer the patient for treatment, if indicated
- Review the treatment regimen
- Ensure that medications are ordered and given at the correct time, and in the correct dosage
- Monitor for side effects and adverse reactions to medication
- Assess adherence daily and monthly, and identify positive and negative motivational factors influencing adherence
- Address 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 TB symptoms, bacteriology reports, radiographic results, weight, vital signs, drug susceptibility results, and comparing them to previous documented findings. This review is an important measurement of clinical improvement, worsening, or stabilization of the patient's condition. The case manager should **collect three (3) sputa** for acid-fast bacilli (AFB) sputum smear and culture **at least every two (2) weeks until sputum smears are negative.** Thereafter, three (3) sputa should be collected at least **monthly until there are three negative cultures**. If a patient is on DOT, no further specimen collected is indicated unless the patient becomes symptomatic again. A clinician should complete a medical evaluation at the time of diagnosis and periodically based on patient condition or review of diagnostic information, patient chart, and chest radiographs. 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 to ensure accuracy. Also, conduct this review at conversion as evidence for the improving condition of the patient.[40]

Inconsistencies should trigger additional questions, such as the possibility of laboratory contamination. Bring these questions immediately to the attention of the health care provider, case manager and Alaska TB Program (907) 269-8000.

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 done 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.[41] 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.[42]

Review the treatment regimen to verify that the physician's orders are clear and that dosages are correct for the patients' age and weight. 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.[43]

For consultation regarding the treatment of TB, contact the Alaska TB Program at 907-269-8000.

Ensure that medications are ordered and given at the correct time, and in the correct dosage. Review the patient's treatment plan and chart, and correct the medications as necessary. Dosages may need to be adjusted if a patient's weight changes.

Monitor the side effects of and adverse reactions to medication. Review laboratory findings and contact the treating physician if abnormal results are obtained.[44] The patient should be asked about adverse reactions to the medication prior to each dose of medication administered by directly observed therapy (DOT). If the patient is symptomatic the DOT Aide should hold medications and notify the PHN case manager as soon as possible. Chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done per orders from the medical provider or medical officer for the Alaska TB Program. See Table 5**: Monitoring and Interventions for Side Effects and Adverse Reactions** in the Treatment of Tuberculosis Disease section **6.15**.

PHN case managers who work with DOT Aides should stress upon DOT Aides the importance of notifying the PHN as soon as possible in these situations:

- The patient misses two (2) or more consecutive DOT doses;
- The patient reports symptoms of medication side effects or adverse reactions

Use the *Referral and Authorization for TB Screening and Follow-up Services* **(18.1)** to refer uninsured patients for a hepatic panel/liver function tests if necessary. The Alaska TB Program will provide partial reimbursement for services as indicated on the form.

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 directly providing DOT, the DOT Aide should alert him or her if the patient misses a DOT dose. If two (2) or more DOT doses are missed, the DOT Aide should notify the PHN case manager as soon as possible. The PHN case manager should contact the patient the same day or the next business day and should reinforce the need for adherence with the DOT plan. Individualized incentives or enablers should be used to promote treatment adherence.

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**.

A preventable interruption in treatment can be avoided if the PHN case manager is notified immediately, rather than when the monthly DOT calendar is submitted. Also, regularly monitor the effectiveness of enhancement methods (i.e., incentives, enablers, behavioral contracting, or behavior modification).[45] The case manager should review the monthly DOT calendars to ensure that patients have taken all medications. The case manager should ensure that the patient is informed about the consequences of nonadherence, including legal interventions. Changes in the patient's attitude toward the healthcare worker and TB regimen should be documented.[46]

For more information, see the "Directly Observed Therapy" and "Legal Orders" topics in this section **10.34** and **10.41**.

Address 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 as needed and until satisfactory recall is obtained.

For more information, see the Patient Education section **13.1**.

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] National CDC guidelines recommend that contact investigation should begin within one week of notification of a smear positive suspect or case and be completed as soon as possible. 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 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 at least monthly by the PHN for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the medications should be held. The Alaska TB Program and the provider should be consulted and the patient monitored more frequently. Chemistries and CBC, AST/ALT, or other tests based on specific drugs should be done per orders

See Table 5**: Monitoring and Interventions for Side Effects and Adverse Reactions** in the Treatment of Tuberculosis Disease section **6.15**.

As is true with all medications, combination chemotherapy for tuberculosis may have adverse reaction, 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. In addition, proper management of more serious adverse reactions often requires expert consultation. [53] The Alaska TB Program medical officer is available for consultations upon request at (907)-269-8000

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 **6.13**.

Use the *Referral and Authorization for TB Screening and Follow-up Services* **(18.1)** to refer uninsured patients for a hepatic panel/liver function tests if necessary. The Alaska TB Program will provide partial reimbursement for services as indicated on the form.

Activities to Monitor for Side Effects and Adverse Reactions

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 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.[54]

For more information, see the Patient Education section **13.1**.

Assess the patient for adverse reactions and side effects. For patients on self-administered therapy, the case manager ensures that patients are assessed for adverse effects to TB medications at least monthly and at each visit. If the patient is on DOT, the PHN or DOT Aide should assess patients 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 .[55]

Monitoring Bacteriologic Improvement

Assess and document response to treatment. The case manager should **collect three (3) sputa for AFB sputum smear and culture at least every two (2) weeks until sputum smear conversion. Thereafter, three (3) sputa should be collected at least monthly until there are three negative cultures.** If a patient is on DOT, no further specimen collected is indicated unless the patient becomes symptomatic. [56]

Activities to Monitor for Bacteriologic and Clinical Improvement

To monitor for response to treatment, perform the activities described below.

Acid-Fast Bacilli Sputum Smear Negative

If a patient is AFB sputum smear negative, place laboratory reports promptly in the patient's chart. If previously AFB sputum smear positive and now AFB sputum smear negative on three separate consecutive days, consider discontinuing isolation.[57]

Acid-Fast Bacilli Sputum Smear Positive

If a patient is AFB sputum smear positive **and**

- **Prior positive:** Place a report in the patient's chart. Repeat sputa smears at least every 2 weeks until three consecutive negative sputa smears have been documented from different days.
- **Has new AFB sputum smear positive results and is diagnosed with pulmonary TB:** Notify the Alaska TB Program and provider and initiate isolation. Repeat sputa smears at least every 2 weeks until three consecutive negative sputa smears have been documented from different days.[58]

Culture-Positive Pulmonary Tuberculosis

For patients with culture-positive pulmonary TB, collect three sputa specimens at least monthly for smears and cultures until persistently negative cultures are documented. [59] Once culture conversion has occurred, discontinue sputa collection.

Continued Positive Sputum Smears or Positive Cultures

If sputum smears or cultures are positive after two months of treatment, call the Alaska TB Program at 907-269-8000 to review the case.

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.

In consultation with the Alaska TB Program, the case manager should initiate the evaluation of the patient and do the following:

1. Review and confirm the patient's medication compliance with the DOT Aide.
2. Reconfirm the appropriateness of the medication regimen, based on drug susceptibility results and other considerations.
3. 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.
4. Consider serum drug levels.
5. Repeat cultures and repeat drug susceptibility testing.[60]

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 improvement.
3. Review and document the patient's symptoms for improvement, if applicable.
4. Review the patient's tuberculin skin testing or IGRA information (retesting may be appropriate if initially negative or if test not initially done), and discuss this with the patient's provider.
5. If the patient is not to be counted as confirmed case of tuberculosis, the Alaska TB Program will classify the patient as a suspect case of tuberculosis. Occasionally, providers may opt to fully treat individuals for culture negative tuberculosis. In these situations, PHN case managers should continue all case management activities as long as the patient is receiving antituberculosis medications for suspected tuberculosis.
6. Discuss the above findings with the Alaska TB Program at 907-269-8000 to determine if the patient is to be reported as a case. Often, determination of status for such clinical cases cannot be done until the end of treatment.

Verification of Isolate Drug Susceptibility Results

The case manager should obtain and promptly document all positive cultures and respective drug susceptibility results.

1. I**f a patient's TB organism is susceptible to all first-line anti-tuberculosis drugs**: Follow the recommended treatment regimen.
2. **If a patient's TB organism is drug resistant**:
   - **a.** Consult with the patient's health care provider and the Alaska TB Program at 907-269-8000.
3. If isoniazid-resistant or multidrug-resistant TB (MDR-TB) or extremely drug resistant TB (XDR-TB):
   - **a.** Place contacts on appropriate latent TB infection (LTBI) treatment regimens. Treatment of LTBI caused by drug-resistant organisms should be provided by, or in close consultation with, an expert in the management of these difficult situations. For patients with MDR-TB, refer to the instructions on multidrug-resistant tuberculosis provided below.

Contact the Alaska TB Program at 907-269-8000 for consultation regarding the treatment of all drug-resistant tuberculosis and management of contacts.

Multidrug-Resistant Tuberculosis

Notify the Alaska TB Controller of all cases of suspected or confirmed MDR-TB or XDR-TB. Consultation regarding the treatment of all drug-resistant tuberculosis and management of contacts is available by calling 907-269-8000.

Clinical Response to Treatment

The case manager should monitor/evaluate a patient's clinical response to treatment. Some indicators are:

1. Lessening or resolution of TB symptoms
2. Weight gain
3. 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. [61]

Criteria for starting isolation and discontinuing isolation are provided in the Infection Control section **17.15**.

Closing a Case

If the patient is not to be reported as a verified case of tuberculosis, the Alaska TB Program will notify the PHN case manager that the patient is categorized as a suspect case of tuberculosis vs. a confirmed case.

For more information on closing a case, see the "Completion of Therapy" topic in this section **10.29**.

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 an Alaska TB Program 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 PHN case manager.

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 and consulting with the Alaska TB Program to ensure that the patient has received an adequate course of therapy.

- **If culture remains positive beyond two months of treatment,** reasons for persistent positive cultures should be examined and treatment adjusted/prolonged.
- **For TB involving the bones or joints or tuberculous meningitis:** These are exceptions to the standard six-month course. See “Duration of Treatment” in the “Treatment Regimens and Dosages” topic in the Treatment of Tuberculosis Disease section **6.11.**
- **HIV-negative, culture-negative patients:** See “Duration of Treatment” in the “Treatment Regimens and Dosages” topic in the Treatment of Tuberculosis Disease section **6.11**.
- **Relapse of TB following treatment for TB with pan-susceptible organisms.** Treatment may be prolonged to nine months or more. (Current drug susceptibility testing must be performed and the regimen adjusted if resistance has developed.)[62]

Calculating Completion of Therapy

Base the completion of treatment on the number of doses of directly observed therapy (DOT) and full weeks of treatment received rather than on the chronological passage of time. Each dose should be recorded on the DOT calendar and counted to ensure that the required number of doses has been delivered and consumed over the course of the number of weeks of treatment.

For the total number of doses recommended for completion of regimens using first-line drugs, refer to the “Treatment Regimens and Dosages” topic in the Treatment of Tuberculosis Disease section **6.6**.

Use the *TB Medication Dose Monitoring* forms to help count each DOT dose. The F Form to assist in counting drugs for all approved regimens can be found in the Forms section of this manual **18.1**.

Contact the Alaska TB Program at 907-269-8000 to determine the end of treatment date based upon the number of DOT doses consumed during the number of weeks of treatment.

Documenting Completion of Treatment and Follow-up Recommendations

The case manager should insure that the patient understands when TB treatment is complete and provide written documentation to the patient of an adequate course of treatment. General and individualized specific follow-up recommendations should also be provided in writing to the patient. All individuals completing treatment for active tuberculosis should also be educated about the symptoms of tuberculosis and be advised to be re-evaluated should they occur in the future.

Use the *End of Treatment Letter and Summary* to provide written TB treatment and follow-up information to the patient. It can be found in the Forms section of this manual **18.1**.

Case Closures Other than Completion of Therapy

- **Moved:** All attempts should be made by the case manager to obtain the new or forwarding address. If this new address is within the original jurisdiction, the case should be transferred, as per the local public health agency protocol. If the new address is in another jurisdiction, the Alaska TB Program should be notified and procedures followed as described in the Transfer Notifications section. Cases should be closed as “moved” only if a new address is obtained.

For information on who to alert when a case will move or has moved, refer to the Transfer Notifications section **15.1**.

- **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.”

If unable to locate a patient despite many attempts, call the Alaska TB Program at 907-269-8000 to review the case.

- **Died:** If the patient expired prior to completion of therapy, the case is closed as "Died."[63]

Ensure that the contact investigation on the case is also completed. For more information, see the Contact Investigation section **11.1**.

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?

The Alaska TB Program conducts monthly case management teleconferences with PHNs. Call 907-269-8000 to schedule.

Evaluation Activities

To evaluate case management, perform the following activities:

- Monitor the multidisciplinary care plan at least monthly
- Identify strengths or weaknesses
- Conduct a case management teleconference at least every month with the Alaska TB Program
- Monitor case reporting and the contact investigation
- Participate in cohort review[64]

Monitor the treatment plan at least every month 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. If the treatment plan has remained unchanged, determine the reason why.[65]

Identify strengths or weaknesses that negatively or positively affect the expected outcome. A good evaluation will lead to positive changes for the patient and others.

Conduct a case management meeting or teleconference with the Alaska TB Program periodically to identify variances or common elements among a group of patients being

evaluated or treated for TB. Case management teleconferences allow a systematic review of the management of TB patients with TB disease and their contacts. With the information learned from the evaluation, the case manager can make changes to improve patient care outcomes.[66]

Monitor reports to ensure that the TB case reports are accurate and updated according to state standards and that the contact investigation is complete.[67]

Cohort review is a systematic review of patients with tuberculosis (TB) disease and their contacts. A “cohort “ of patients from a specific period of time (usually 3 months) is reviewed in terms of individual patient outcomes and program performance. Thus it is a management process used to increase staff accountability for patient outcomes including completion of treatment for both TB disease and LTBI, improve TB case management and identification of contacts, motivate staff, identify program strengths and weaknesses, and determine staff training and professional education needs. Increased accountability also helps TB control programs meet their program objectives and national objectives.[68]

In lieu of cohort review, the Alaska TB Program uses monthly case management meetings and teleconferences with PHN case managers and select providers to ensure that all patients receive appropriate care and management in order to achieve the best possible outcomes for persons being treated for suspected or confirmed tuberculosis and for high risk individuals being treated for LTBI.

Directly Observed Therapy

Provide directly observed therapy (DOT), as required. DOT means that a healthcare worker or other designated individual trained and monitored by the PHN case manager 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. All patients on SAT should be monitored at least monthly for adverse reactions. Ideally, this should occur at the time that medications are dispensed.

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 Alaska TB Program recommend that every tuberculosis (TB) patient be given medication via DOT.[69] 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;[70] 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 is the standard of care for all pulmonary and laryngeal TB cases and suspects, both nationally and in Alaska. The goal of the Alaska TB Program is to place all patients on DOT regardless of the patient's circumstances because it has been shown to be such an important treatment tool.[71] DOT is recommended for extrapulmonary TB as well. Additionally, consider DOT for the following:

- Persons with human immunodeficiency virus (HIV) coinfection and on treatment for latent TB infection (LTBI)
- Immunocompromised persons on treatment for LTBI
- Contacts under the age of 5 on treatment for LTBI
- Contacts who are TST converters and on treatment for LTBI
- All individuals on the 12-week INH/RPT regimen for LTBI **must** have DOT.

Three times weekly doses of TB medications should be scheduled on Monday, Wednesday and Friday to insure that the prescribed regimen is delivered by DOT.

Face-to-Face and Video DOT

The standard of care for DOT in Alaska is a face-to-face visit between the patient and PHN or DOT Aide. Although some TB Programs are using video DOT (VDOT) for treatment of select, low risk patients, this is **not** an option in Alaska at this time. A number of challenges must be addressed before VDOT is approved in Alaska including identifying a secure, HIPAA-compliant application (DHSS does not consider Skype or FaceTime to be compliant) at reasonable cost, development of policies and procedures, and pilot testing before full implementation.

VDOT has been shown to reduce staff costs and travel time, increase patient and staff satisfaction with treatment, allows patients greater freedom and flexibility and increases the likelihood of treatment completion.[72] It is anticipated that it will be an option for DOT in the future.

How to Deliver Directly Observed Therapy

In Alaska, PHN case managers are responsible for recruiting, training, and monitoring the work of DOT Aides.

The TB/LTBI Prescription and Medication Request Guidelines contain detailed information on ordering and storing antituberculosis medications. It is available in the Forms section of the manual **18.1**.

The Alaska TB Program has a detailed DOT Manual and training video posted on its website. These materials were developed as a collaborative project between the Alaska TB Program and the Section of Public Health Nursing. http://dhss.alaska.gov/dph/Epi/id/Pages/tb.aspx

Who Can Deliver Directly Observed Therapy?

- PHNs or other clinical staff, such as a nurse or other healthcare worker
- Staff at other healthcare settings, such as outpatient treatment centers
- Other responsible persons, such as school personnel, employers, others trained by the PHN case manager
- DOT Aides in Alaska
- *Not* immediate family members[73]

DOT Aides, Regimens, and Payment for DOT Services

DOT Aides

PHN case managers are responsible for organizing and managing DOT. These responsibilities include identifying, hiring, training, and monitoring the work of DOT Aides. The patient and DOT provider should agree upon the time and place for DOT encounters. Sites might include a clinic, workplace, public meeting place such as a restaurant, or the patient's home. In addition to providing DOT and documenting all doses according to guidelines, the DOT Aide also reports symptoms of adverse reactions, missed doses, and anticipated patient travel to the PHN case manager. DOT can be provided by PHN staff, CHA/CHAPs, teachers, workplace safety officers and other reliable adults. Immediate family members should only be considered as DOT Aides when all other options have been exhausted and must be approved by the Alaska TB Program.

DOT Regimens

The Alaska TB Program recommends the use of TB treatment regimens contained in the Treatment of Tuberculosis Disease section **(6.6 – 6.12)**. When DOT is used, drugs may be given five (5) days a week and will be considered to be daily dosing[74] The Alaska TB Program does not expect that TB medications will be provided by DOT Aides, PHNs, or others on weekends and will only provide payment to DOT Aides for up to 5 doses of anti-TB medications per patient each week unless pre-approved. Some providers may prescribe antituberculosis medications seven (7) days a week. In such situations, medications will be left with the patient to self-administer during the weekend but these doses will **not** include in the final dose count since they were not administered by DOT.

Payment for DOT Services

PHN staff is never paid to provide DOT to patients; it is considered part of their job duties. Similarly, in situations where CHAPs administer DOT during their normal work hours they should not be offered payment for DOT. When CHAPs make home visits or meet the patient for DOT after hours or during their lunch break, they may be eligible for DOT payment if arranged in advance with the Alaska TB program. The Alaska TB Program provides payment to DOT Aides for each day they deliver and observe the patient swallow their TB medications.

Funding for DOT Aides is very limited and must be used wisely. Patients with active TB disease remain the first priority for DOT. However, certain individuals with LTBI should also be considered for DOT based on the risks described above. All individuals on the 12-week INH/RPT regimen for LTBI must have DOT.

Use the *DOT Aide Job Description*, *DOT Aide Memorandum of Agreement, DOT Calendar,* and *DOT Monthly Invoice for Payment* **(18.1)** to document activities. Send copies of the completed *DOT Calendar* and *DOT Monthly Invoice for Payment* to the Alaska TB Program to request monthly payment for DOT services.

The Alaska TB Program will only provide payment to DOT Aides for up to 5 doses of anti-TB medications per patient each week unless pre-approved. If the provider wants medications to be taken 7 days a week, it is acceptable for most patients to self administer weekend doses. Only doses delivered by DOT will be counted to determine the completion of treatment date.

Principles of Directly Observed Therapy

- The healthcare worker or DOT Aide should watch the patient swallow each dose of medication. This is done during a face-to-face encounter.
- Use DOT with other measures such as incentives and enablers to promote adherence.
- DOT can be given anywhere the patient and healthcare worker or DOT Aide agree upon, provided the time and location are convenient and safe.[75,76]

Directly Observed Therapy Tasks

1. Obtain antituberculosis medications from the PHN and ensure that they are stored safely and out of the reach of children at all times. Dose packs are NOT child proof and must be stored securely.
2. Deliver medication.
3. Check for side effects and adverse reactions prior to each observed dose.

For more information, see the "Ongoing Assessment and Monitoring" topic in this section **(10.20)** and the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section **6.13.**

4. Verify medication.
5. Watch the patient swallow pills.

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.[77]

6. Document the visit.

Use the *DOT Calendar* **(18.1)** to record each dose of medication given via DOT.

7. As necessary and appropriate, do the following:

a. Provide patient education

b. Help the patient keep appointments

c. Offer incentives and/or enablers to encourage adherence[78]

For more information, refer to the Patient Education section **(13.1)** and the "Incentives and Enablers" topic in this section **10.40**.

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.[79]

For more information, see the Patient Education section **(13.1)**. 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 .

Agreements

It may be useful to develop a treatment contract or acknowledgment between the patient and the DOT worker. Some jurisdictions have successfully used these 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.[80]

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 **10.40**.

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. The PHN case managers should notify the Alaska TB Program if a patient misses two (2) or more consecutive doses.

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 education efforts appropriate to the individual patient.

Incentives and Enablers

Use incentives and enablers to enhance adherence to therapy.[81] Incentives and enablers are used to improve patient attitudes and to foster good health behaviors.[82] They help patients stay with and complete treatment.[83]

Incentives are small rewards given to patients to encourage them to adhere to their treatment plan and keep their clinic or field directly observed therapy (DOT) appointments.[84] **Enablers** are those things that make it possible or easier for the patients to receive treatment by overcoming barriers such as transportation difficulties. An incentive that works for one patient may not work for another. Whenever possible, it is advisable to identify and use incentives and enablers that will effectively motivate or assist each unique patient to complete treatment.[85]

The Alaska TB has very limited funding for incentives and enablers. **Patients undergoing treatment for active TB are always the highest priority for incentives and enablers to keep them adherent to their TB treatment regimens.** As funding permits, patients being treated for LTBI may also be offered incentives and enablers to encourage completion of treatment.

Table 1: EXAMPLES OF INCENTIVES AND ENABLERS

Incentives	Enablers
Food and beverages Clothing Automotive supplies Hobby/craft items Household items Laundry services Seasonal/holiday treats Movie passes, movies by mail (Netflix) Restaurant/fast food vouchers Toys Personal care items Gift Cards	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 or utility assistance Assisting the client to complete paperwork to get food/housing assistance Assisting the client to get substance treatment

To obtain incentives and enablers, see the "Incentives and Enablers" topic in the Supplies, Materials, and Services section **(16.1)**. PHNs should consult their Regional Nurse Managers (RNMs) to request funds for incentives and enablers.

Medical Orders

Progressive Interventions

Nonadherent adults with infectious pulmonary TB pose the greatest threat to the health of a community. Progressive intervention should begin after learning the possible reasons for nonadherence and addressing the identified problems using methods such as education, directly observed therapy (DOT), incentives, and enablers. The patient should be told orally and in writing of the importance of adhering to treatment and the consequences of failing to do so.[86] It is advisable to have patients sign a contract or treatment agreement acknowledging plans for isolation, DOT arrangements, etc.

The Alaska TB Program may work with the Attorneys' General Office to pursue medical orders for persons suspected or diagnosed with TB who do not adhere to recommendations for examination, TB treatment, or isolation. This is done on a case-by-case-basis and **only** after all attempts at least restrictive alternatives have been attempted. PHN case managers must maintain detailed documentation of all written contracts or verbal agreements with patients, use of incentives and enablers, attempted contacts and patient response, including failure to maintain isolation and/or keep appointments or DOT encounter agreements.

For Alaska State laws on tuberculosis (TB), see the Statutes and Regulations section **19.1**.

Use the *Tuberculosis Treatment Contract* to document written agreements with the patient regarding isolation, DOT, etc. It can be found in the Forms section of this manual **18.1**.

Resources and References

General Case Management Resources

Curry International Tuberculosis Center. *Asking the Right Questions:A Visual Guide to Tuberculosis Case Management for Nurses* (Curry International Tuberculosis Center website) 2010. Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=ONL-14

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Directly Observed Therapy Resources

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Incentives and Enablers Resources

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Contact Investigation

CONTENTS

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

- 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 (younger than 5 years of age or immunocompromised); and
  - 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 Alaska guidelines to do 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 Alaska 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 to achieve the goal of reduction of TB morbidity and mortality is prompt identification of contacts of 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 in protecting 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 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.[6] A study showed that improvements in contact investigations might have prevented 17 (10%) of 165 pediatric TB cases in California in 1994.[7]

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 pleural disease with either

- pulmonary cavities;
- respiratory specimens that have acid-fast bacilli (AFB) on microscopy; or
- especially both.[8]

Persons with AFB sputum smear negative results are less likely to be infectious, but are still capable of infecting others.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18.**

Program Standards

Contact and source case investigations
Public health nurses are responsible for doing contact and source case investigations. Contacts of tuberculosis cases and suspects should be investigated according to the protocol in this section. The public health nurse should begin this investigation as soon as possible after being notified of a suspected or confirmed case of tuberculosis disease.

A source-case investigation seeks the source of recent *M. tuberculosis* infection, perhaps newly diagnosed TB disease. Associates of children <5 years of age diagnosed with tuberculosis should be evaluated in an effort to identify the source of infection. In addition, source-case investigations may be done for children <2years of age who are diagnosed with LTBI.

Forms

For each investigation, complete the *Contact Investigation Form* in the Forms section **(18.1)**. Also see the Required Reports from Local Public Health Agencies to the Alaska TB Program" topic in the Surveillance section **2.10**.

Persons with AFB sputum smear negative results are less likely to be infectious, but are still capable of infecting others.

Reporting and recordkeeping requirements: Initial and final results of contact or source case investigations must be forwarded to the Alaska TB Program. Staff from the Alaska TB Program will work with public health nurses to assess the completeness of the contact investigation. The results of the follow-up skin tests should also be documented and forwarded to the Alaska TB Program. See Table 4: **Overview of Ongoing Management Activities and Maximum Time Frames (11.17)** for timelines.

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 for contacts
8. Decision about whether to expand testing
9. Evaluation of contact investigation activities[9,10]

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.[11]

Contact Investigation Plan

The investigation plan starts with information gathered during interviews and site visits. It should include a list of the contacts, their assigned priorities, and a written timeline. The timeline sets expectations for monitoring the progress of the investigation, and it informs public health officials about whether additional resources are needed for finding, evaluating, and treating the high- and medium-priority contacts.

For more information on timelines, see Table 2: **Time Frames for Investigating the Index Patient and the Sites of Transmission (11.13)** and Table 3: **Time Frames for Contact Evaluation and Treatment (11.15)** in this section's topic "Time Frames for Contact Investigation."

The plan is a work in progress which is subject to revision if additional information indicates a need to expand a contact investigation. It is part of the permanent record of the overall investigation for later review and program evaluation.[12]

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, public health officials 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 on 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.[13]

Table 1. INDEX PATIENT FACTORS INCREASING TRANSMISSION RISK [14]

Characteristics of the Index Patient	Behaviors of the Index Patient
Pulmonary, laryngeal, or pleural tuberculosis (TB)	Frequent coughing
Positive acid-fast bacilli sputum smear results	Sneezing
Cavitation on chest radiograph	Singing
Adolescent or adult patient	Close social network
Lack of treatment or ineffective treatment of TB disease	

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 their infection. For contact investigations, 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.[15] 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 of age 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 needs to be done 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.[16] 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.[17] Regardless of known HIV status, HIV counseling should always be recommended for all patients as a part of the screening process.[18]

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 sputa and by observing infection rates in household contacts. However, the exact rate of decrease cannot be predicted for individual patients, and an arbitrary determination is required for each.

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.

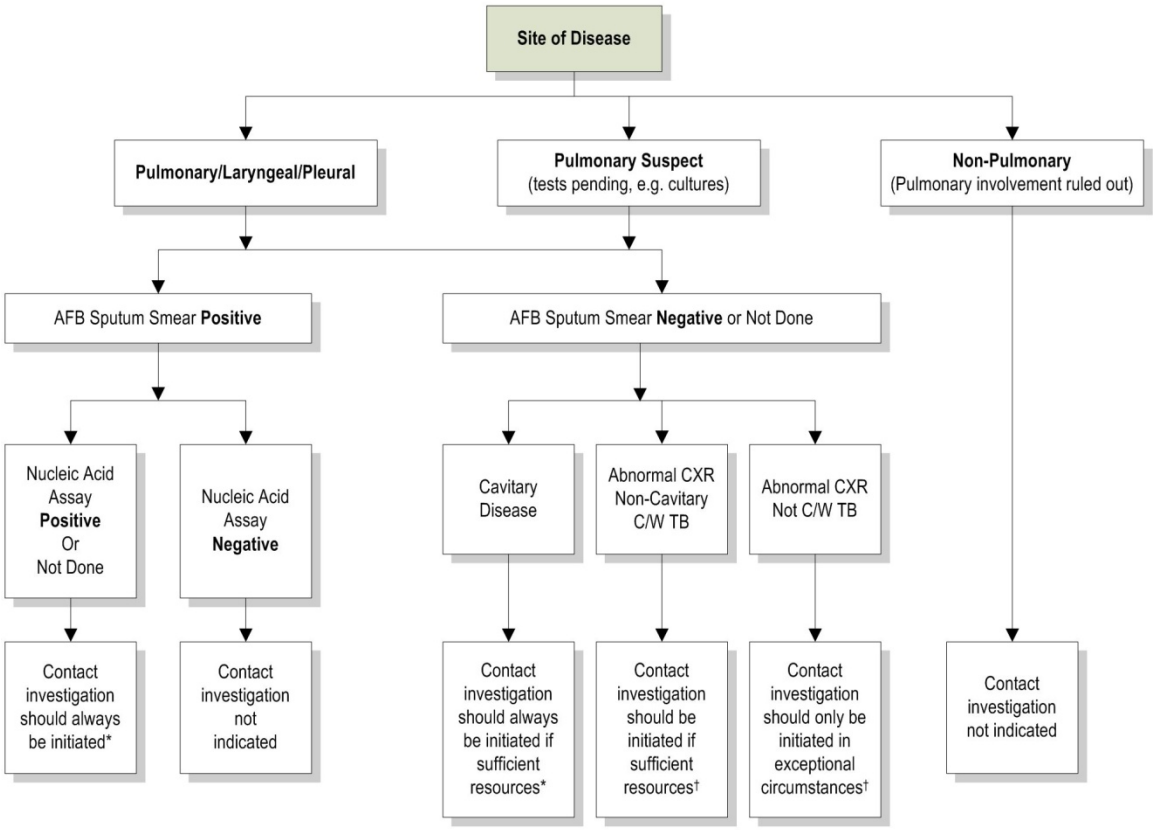
For more information on drug-resistant tuberculosis see the Treatment of Tuberculosis section **6.22**.

Resistance to only isoniazid (INH) leaves the option of four months of daily rifampin (RIF), but additional resistance to RIF constitutes multidrug-resistant TB (MDR-TB). If this is the case, all the potential regimens are poorly tolerated to some extent, while none of these regimens have been tested fully for efficacy

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[19]



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 TB suspect. Although sputum smear-positive pulmonary, laryngeal or pleural TB suspects may turn out to have nontuberculous mycobacteria (NTM) instead of *M. tuberculosis,* opportunities for appropriate contact investigation may be delayed, or even lost, if the PHN waits 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".

For patients whose samples were reported smear or culture positive at other laboratories, providers and PHN case managers should collect and submit sputum specimens on TB suspects to the Alaska State Public Health Laboratory (ASPHL). Doing so facilitates more rapid completion of testing and provides an isolate to be sent for universal genotyping.

When sputum samples have not been collected, either because of an oversight or the patient's inability to expectorate, 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.

A contact investigation can 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.

  For more information on outbreak investigations, see the "Outbreak Investigation" topic in this section **11.47**.

- **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. Source case investigations should always be done when children under the age of 5 are suspected or are diagnosed with TB. Source case investigations may also be done when children under the age of 2 are diagnosed with LTBI.

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 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, 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 (11.13)** for the recommended time frames for index patient interviews and visits to the residence transmission sites.

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 on the characteristics of the index patient as well as the duration and circumstances of the exposure, and the vulnerability/susceptibility of the contacts to disease from *Mycobacterium tuberculosis* infection (such as contacts < 5 years of age or HIV infection, immunosuppression or underlying disease processes).

For information on how to determine which contacts are high, medium, and low priority, see the “Contact Priorities” topic in this section **11.27**.

Table 2: TIME FRAMES FOR INTERVIEWING THE INDEX PATIENT[20]

Activity	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.

Circumstances unique to Alaska may prevent meeting the contact investigation timelines in CDC's national standards. Interviews and contact investigation activities should be initiated as soon as possible for persons with suspected or confirmed TB disease.

When patients are hospitalized or reside outside of their home community at the time of diagnosis, consult the Alaska TB Program at 907-269-8000 regarding options for timely initiation of contact investigation.

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 is based on the likelihood of infection and the potential hazard to the individual contact if infected.[21] For information on how to determine which contacts are high-, medium-, or low-priority, see the "Contact Priorities" topic in this section **11.27**.

Table 3: TIME FRAMES FOR CONTACT EVALUATION AND TREATMENT[22]

Type of Contact	Business Days from Listing of a Contact to Initial Encounter*	Business Days from Initial Encounter to Completion of Medical Evaluation†
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[23]	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[24]	10 Business Days
Medium-Priority Contact Regardless of AFB sputum smear or culture result	3 Business Days After Being Listed in the Investigation[25]	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.

Circumstances unique to Alaska may prevent meeting the contact investigation timelines in CDC's national standards. Interviews and contact investigation activities should be initiated as soon as possible for persons with suspected or confirmed TB disease.

CDC recommendations include the use of interferon gamma release assays (IGRA) in all instances, including contact investigation, where tuberculin skin test (TST) would be used. For children under the age of 5 years, TST is the preferred method of screening.[26]

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 when to decide whether to expand the investigation.

Table 4: OVERVIEW OF ONGOING MANAGEMENT ACTIVITIES AND RECOMMENDED TIME FRAMES[27]

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*
Document all initial contact investigation activities and submit forms to the Alaska TB Program	To ensure that contacts documented, appropriate and complete medical follow-up has occurred, and high-risk contacts identified and treated	10 business days after index case reported to PHN case manager
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) if contact is initially TST-negative	To determine if contact has converted	8 to 10 weeks after each contact's initial TST or last exposure to the index patient†

Activity	Purpose	Maximum Time Interval
Reevaluate contacts who were initially TST-negative and started on LTBI treatment (Consider Window Period Treatment for select high priority contacts)	To determine if treatment for LTBI should be continued	8 to 10 weeks after each contact's initial TST or last exposure to the index patient before the end of the infectious period†
Document all repeat TSTs and follow-up and submit forms to the Alaska TB Program.	To ensure that contact list complete, appropriate and complete medical follow-up has occurred, and high-risk contacts identified and treated	Submit documentation of follow-up within 10 business days.
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
Identify/evaluate issues that 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	To provide epidemiologic analysis of investigations and to measure performance using indicators that reflect performance objectives[28][29]	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: In rare circumstances, an infectious index patient with advanced disease can stay infectious for several months. In these circumstances, the second TST 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 negative and have continued exposure to the infectious index patient should have a third TST 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 on 3/12/2007. The last date the index patient was infectious was 3/5/2007. The household member should have a third TST 8 to 10 weeks from 3/5/2007. For consultation regarding the appropriateness of a third TST, call the Alaska TB Control at 907-269-8000.

Source: Adapted from: California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA). Guidelines for the Investigation of Contacts of Persons with infectious Tuberculosis. *CDHS/CTCA Joint Addenda* [CTCA Web site]. *2011*. Available at: http://ctca.org/filelibrary/ctcaciguidelines117_.pdf. Accessed January 9, 2017.

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).[30] The start of the infectious period cannot be determined with any current methods, so a practical estimation is necessary. From expert opinion, an assigned start three months prior to TB diagnosis 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 are the approximate dates that TB symptoms were noticed, bacteriology results, and the extent of disease—especially the presence of large lung cavities, which imply prolonged illness as well as infectiousness.

Use Table 5: **Guide for Estimating the Beginning of the Period of Infectiousness** to determine the start of the infectious period.

Table 5: GUIDE FOR ESTIMATING THE BEGINNING OF THE PERIOD OF INFECTIOUSNESS[31]

Characteristics			
TB symptoms	AFB* sputum smear positive	Cavity chest radiograph	Recommended minimum beginning of likely period of infectiousness
Yes	No	No	3 months before symptoms onset or first positive finding (e.g., abnormal chest radiograph) consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptoms onset or first positive finding consistent with TB disease, whichever is longer
No	No	No	4 weeks before date of suspected diagnosis
No	Yes	Yes	3 months before 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 the 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 exposure to contacts has ended **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 has three (3) sputum-smears that are (-) for acid fast bacilli.[32,33]

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).

Please consult the Alaska TB Program at 907-269-8000 when clearing patients for travel or return to group settings.

- Generally, a patient may be cleared to travel on a commercial conveyance, return to a congregate living setting or to any setting in which susceptible persons might be exposed **all three** of the following criteria for noninfectiousness have been met:[34]
    1. Has been on antituberculosis therapy for at least two weeks;
    2. Exhibits clinical improvement; and
    3. Has at least three consecutive negative AFB sputum smear results from sputum collected more than eight hours apart (with one specimen collected during the early morning).

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 specific care for the 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 is at home, to obtain further information and answer additional questions.[35]

TB Interviewing for Contact Investigation: A Practical Resource for the Healthcare Worker (Rutgers Global Tuberculosis Institute; 2015) at http://globaltb.njms.rutgers.edu/downloads/products/tbinterviewing.pdf offers specific suggestions on how to prepare for and conduct the interviews.[36]

Record information on the index patient and contacts on *Contact Investigation Form* available in the Forms section of this manual **18.1**.

Preinterview Preparation

Gather information on the patient and the circumstances of the illness to prepare for the first interview.

Consult these sources:

- Current medical record
- Physician who reported the case
- Infection control nurse (if the patient is hospitalized)

The Privacy Rule in the Health Insurance Portability and Accountability Act (HIPAA) permits disclosure of medical record information to public health authorities.[37]

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 health department staff or other persons who may assist in congregate settings to most efficiently ascertain 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 to accurately structure the contact investigation.[38]
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; 2003) at: http://www.currytbcenter.ucsf.edu/node/165

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/component/jsfsubmit/showAttachment?tmpl=raw&id=00Pd00000077hZVEAY

Field Investigation

A field investigation includes visiting the patient's home or shelter, workplace (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 in which exposure occurred. The field investigation may provide additional information for the risk assessment and identify additional contacts.[39]

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 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.[40]
- **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, screen and skin test high- and medium-priority contacts** who are present and arrange for reading of the results.
- **For contacts who are (+) TST**, symptom screening and collection of 3 sputa are advised.
- **Educate the contacts** about the purpose of a 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 for a medical evaluation, including sputum collection.[41]

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.[42]

For more information on infection control, see the Infection Control section **17.1**.

Another critical consideration during field investigations is safety. Healthcare workers should become familiar with policies and recommendations of local law enforcement agencies and health department administration regarding personal safety. Current information on 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 identity badge with a current photo
- Working in pairs when visiting a potentially dangerous area
- Informing someone of your itinerary and expected time of return, especially if you anticipate problems[43]

Contact Priorities

Assign priorities to contacts, using the list 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.[44] Priority-ranking contacts for investigation is based on 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.[45]

Use the assigned priorities to allocate resources to complete all investigative steps for the high- and medium-priority contacts.[46] Dividing contacts into these three levels provides a system for public health staff to reach high-priority contacts first, and then medium-priority contacts, and then 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 recent *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 had TB disease (i.e., vulnerable contacts).[47]

Timely initiation of treatment is especially important for susceptible and vulnerable contacts. Refer to Table 3: **Time Frames for Contact Evaluation and Treatment (11.15)** in the “Time Frames for Contact Investigation” topic.

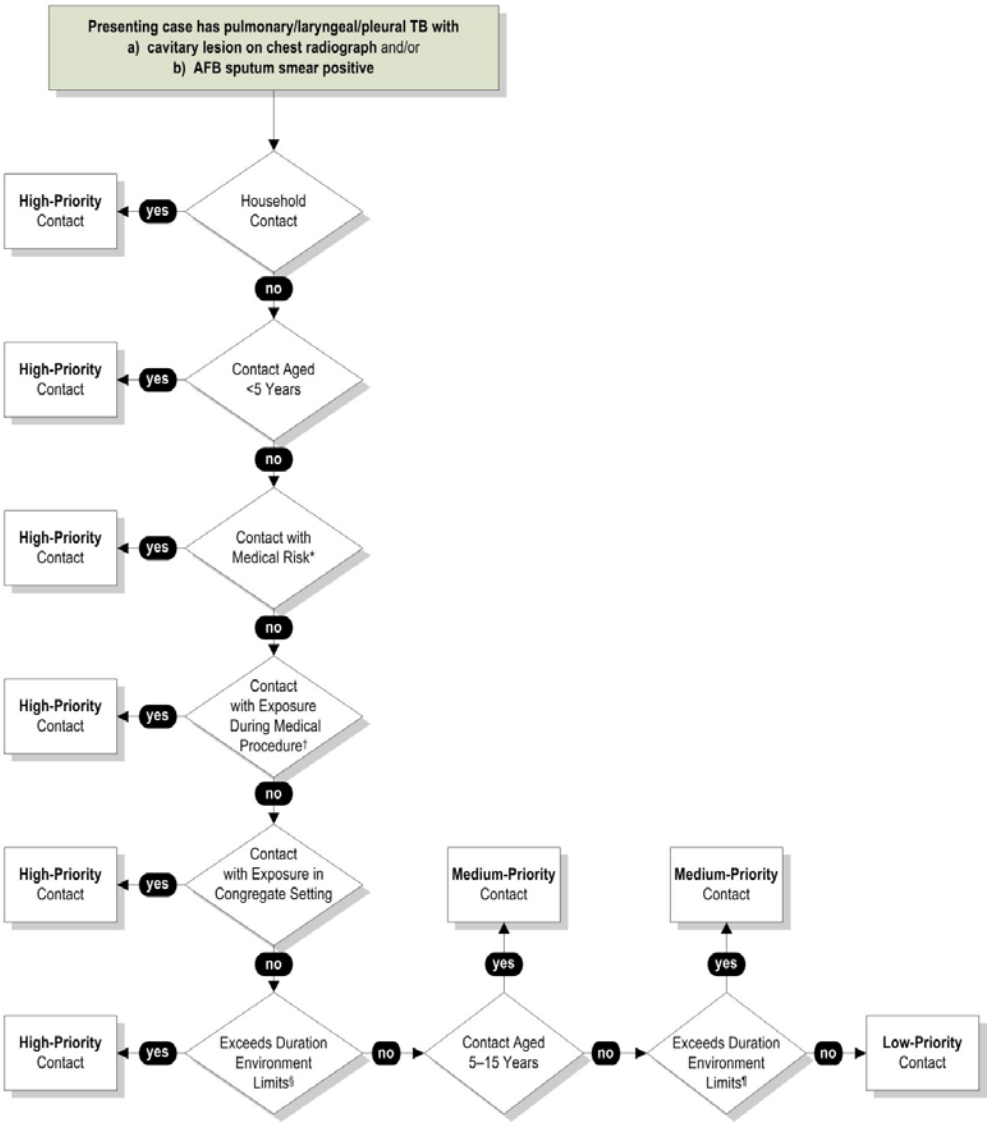
Use the tables on the following pages to assign priorities to contacts to the following:

- Figure 2: **Prioritization of Contacts to Smear-Positive or Cavitary Cases (11.28)**
- Figure 3: **Prioritization of Contacts to Smear-Negative Cases (11.30)**
- Table 6: **Prioritization of Contacts to Cases** with Negative Bacteriologic Results and Abnormal Chest Radiographs Not Consistent with Tuberculosis **(11.31)**

Index Patient with Positive Acid-Fast Bacilli Sputum Smear Results or Cavitary Tuberculosis

Use Figure 2 to prioritize contacts to smear-positive or cavitary index patients.

Figure 2: PRIORITIZATION OF CONTACTS TO SMEAR-POSITIVE OR CAVITARY CASES[48]



Definition of abbreviations: AFB = acid-fast bacilli; HIV = human immunodeficiency virus.

* HIV or other medical risk factor.

† Bronchoscopy, sputum induction, or autopsy.

§ Exposure exceeds duration/environment limits per unit time established by the health department for high-priority contacts.

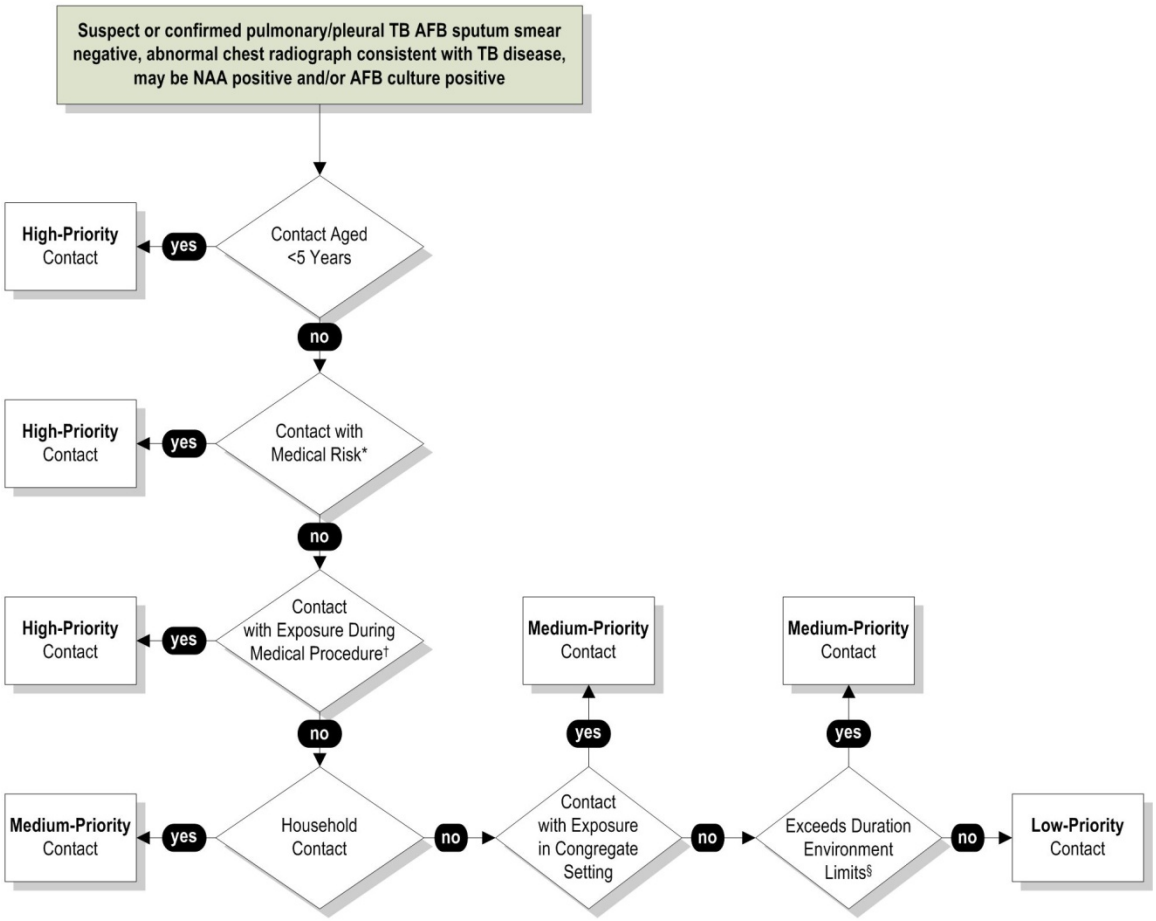
¶ Exposure exceeds duration/environment limits per unit time established by the health department for medium-priority contacts.

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 Figure 3 to prioritize contacts to smear-negative index patients.

Figure 3: PRIORITIZATION OF CONTACTS TO SMEAR-NEGATIVE CASES[49]



Definition of abbreviations: AFB = acid-fast bacilli; HIV = human immunodeficiency virus; NAA = nucleic acid assay.

* HIV or other medical risk factor.

† Bronchoscopy, sputum induction, or autopsy.

§ Exposure exceeds duration/environment limits per unit time established by the local TB control program for medium-priority contacts.

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 6 to prioritize contacts to a suspected case of pulmonary TB who is acid-fast bacilli (AFB) sputum smear negative, and culture negative, and who has abnormal chest radiographs not consistent with TB disease.

Table 6: PRIORITIZATION OF CONTACTS TO CASES WITH NEGATIVE BACTERIOLOGIC RESULTS AND ABNORMAL CHEST RADIOGRAPHS NOT CONSISTENT WITH TUBERCULOSIS[50]

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 usually administered.
- IGRAs can be used in place of (but not in addition to) TST in all situations in which CDC recommends TST as an aid in diagnosing *M. tuberculosis* infection, with preferences and special considerations noted below. This includes contact investigations, testing during pregnancy, and screening of health care workers and others undergoing serial evaluation for *M. tuberculosis* infection. Despite the indication of a preference, use of the alternative test (FDA-approved IGRA or TST) is acceptable medical and public health practice. Caution in interpretation should be used when testing certain populations because of limited data on the use of IGRAs (see Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection, United States)
- Populations in which IGRAs are preferred for testing:
    - Persons who have received BCG (either as a vaccine or for cancer therapy); and
    - Persons from groups that historically have poor rates of return for TST reading.
- TST is preferred over IGRAs for testing children less than 5 years of age.
- Medically evaluate each high- and medium-priority contact to determine whether tuberculosis (TB) disease or latent tuberculosis infection (LTBI) is 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). For recommended time frames, refer to Table 3: **Time Frames for Contact Evaluation and Treatment** (**11.15)** in the "Time Frames for Contact Investigation" topic.
- 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 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.[51]

Use the figures on the following pages to determine the evaluation activities for contacts in these different risk groups and priority rankings:

- Figure 4: **Immunocompromised Contacts and Children Younger than 5 (11.33)**
- Figure 5: **Immunocompetent Adults and Children 5 and Older (High- and Medium-Priority Contacts) (11.35)**
- Figure 6: **Contacts with Prior Positive Tuberculin Skin Tests**

During contact evaluation, treatments, and follow-up, use the *Contact Investigation Form* available in the Forms section of this manual **18.1.**

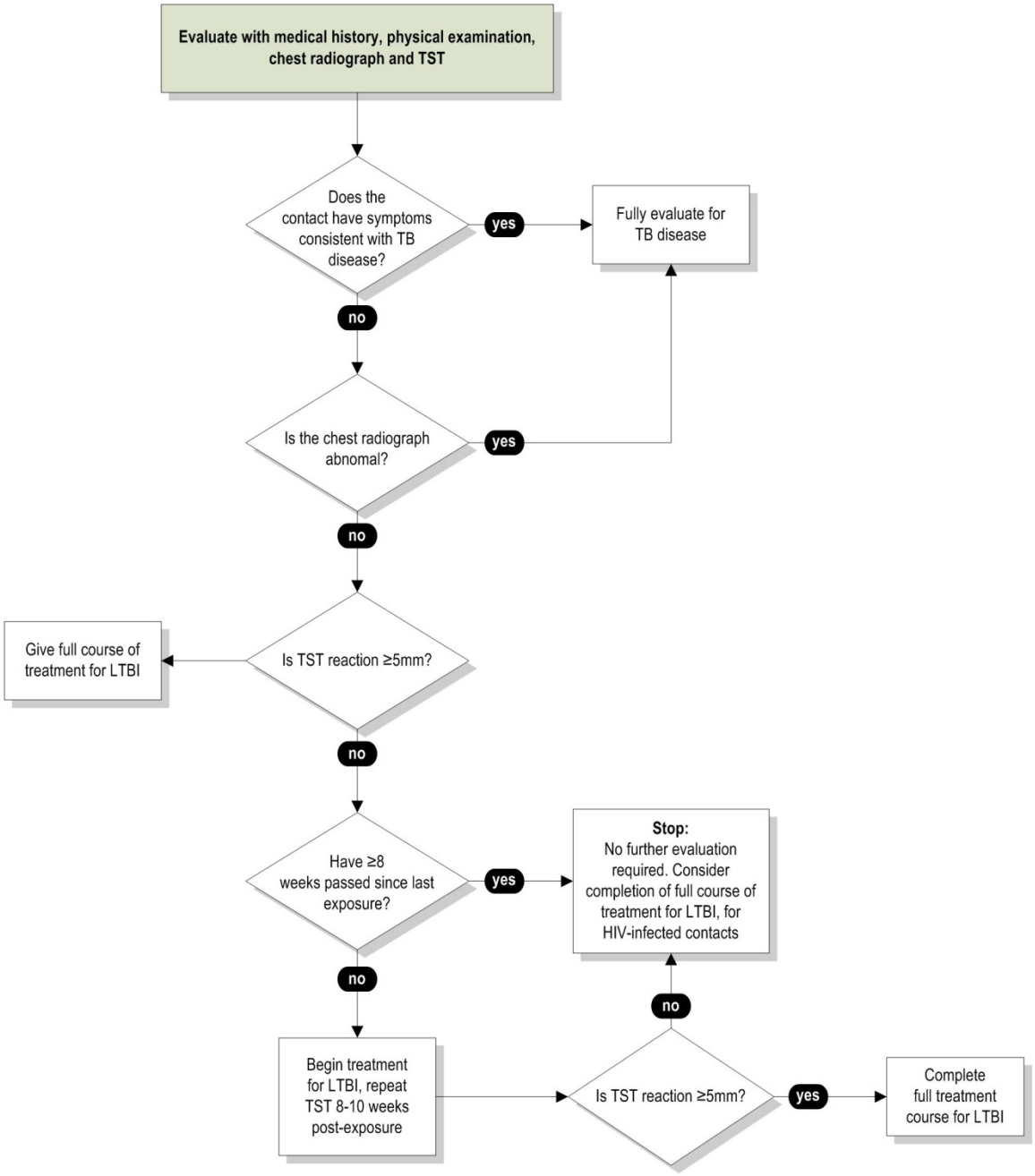
For time frames, see the "Time Frames for Contact Investigation" topic in this section. To arrange follow-up with public health officials in other jurisdictions for out-of-area contacts, see the Transfer Notifications section **15.1**.[52]

IGRAs may be used instead of TSTs in contact investigations EXCEPT in children under 5 years of age where TST is preferred. Unfortunately the Alaska TB Program and PHNs are unable to provide or pay for IGRA testing at this time.

Immunocompromised Contacts and Children under 5

Use Figure 4 to select evaluation, treatment, and follow-up activities for contacts who are immunocompromised and/or under 5 years old.

FIGURE 4: EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPROMISED CONTACTS AND CHILDREN UNDER 5 YEARS OLD[53]



Definition of abbreviations: HIV = human immunodeficiency virus; IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; 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):15.

Evaluate contacts who are immunocompromised or under 5 years of age with medical history, physical examination, chest radiograph, and tuberculin skin test (TST) or interferon gamma release assay (IGRA). Based on the results of these evaluations, take the actions in Figure 4.

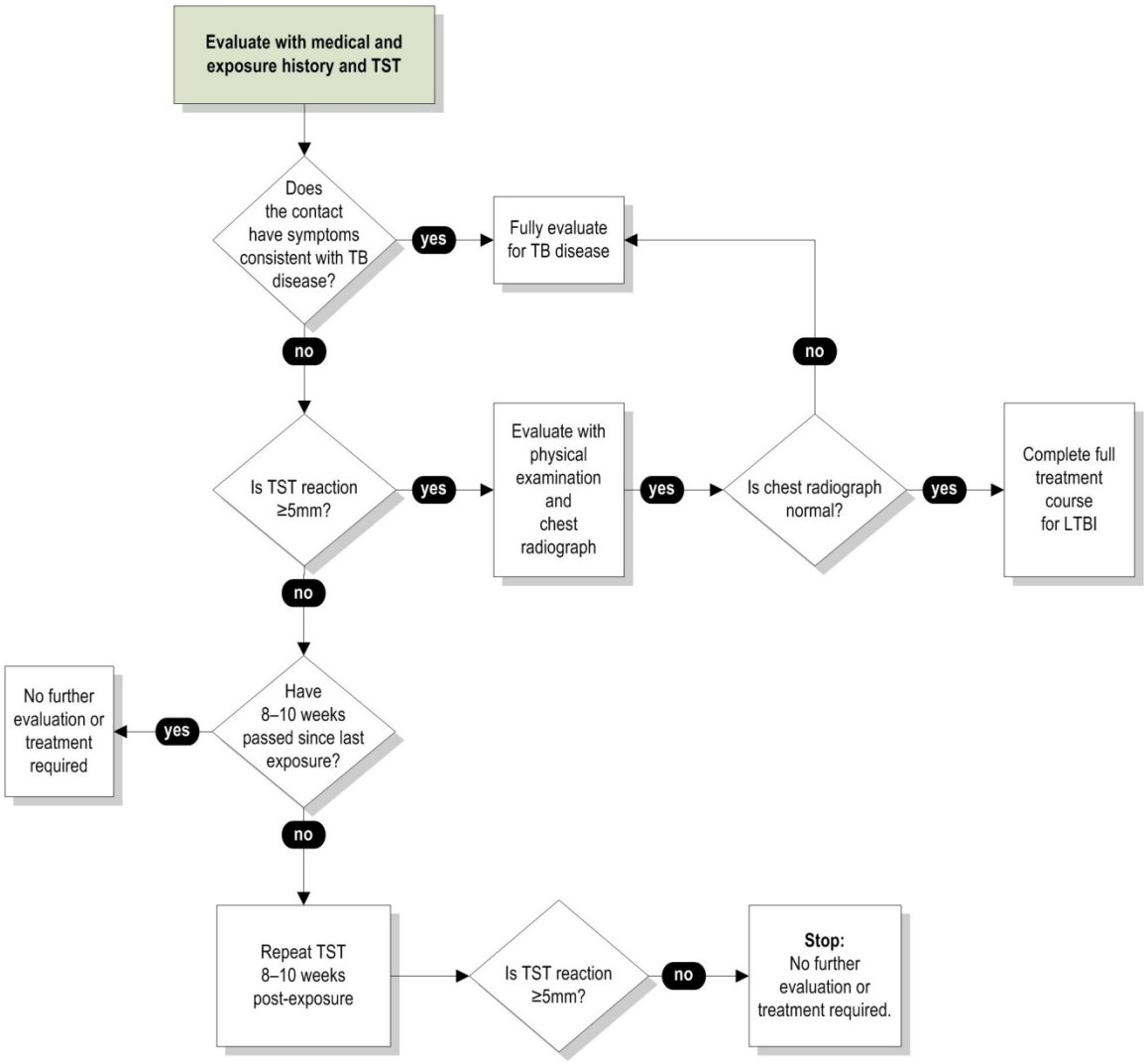
Timely initiation of treatment is especially important for these contacts. Refer to Table 3: **Time Frames for Contact Evaluation and Treatment** in the "Time Frames for Contact Investigation" topic.

Immunocompetent Adults and Children 5 and Older (High- and Medium-Priority Contacts)

Use Figure 5 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 high- and medium-priority contacts who are immunocompetent and/or 5 years of age or older, with medical history, exposure history, and tuberculin skin test (TST) or interferon gamma release assay (IGRA). Based on the results of these evaluations, take the actions in Figure 5.

Figure 5: EVALUATION, TREATMENT, AND FOLLOW-UP OF IMMUNOCOMPETENT ADULTS AND CHILDREN FIVE YEARS OR OLDER (HIGH- AND MEDIUM-PRIORITY CONTACTS)[54]



Definition of abbreviations: IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; TST = tuberculin skin test.

Note: An IGRA may be used in place of a TST.

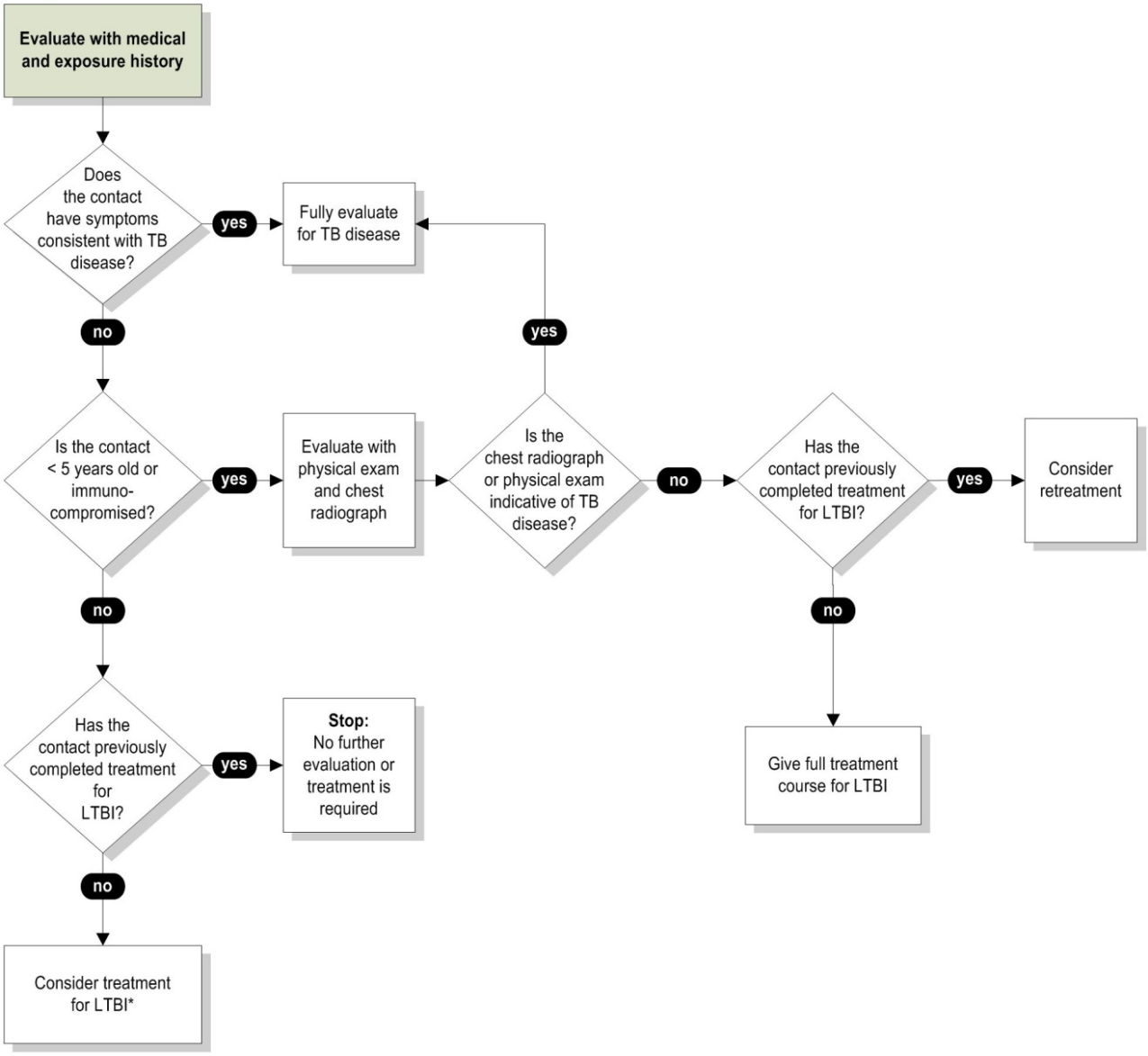
Source: CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis; recommendations from the National Tuberculosis Controllers Association and CDC, and guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):17.

Contacts with Prior Positive Tuberculin Skin Tests

Use Figure 6 to select evaluation, treatment, and follow-up activities for contacts who have prior positive TSTs. For contacts with prior positive TSTs, evaluate them with medical and exposure history. Based on these histories, take the actions in Figure 6.

In Alaska, many contacts to TB suspects and cases have prior positive TSTS and must have their exposure and medical history assessed per Figure 6. Symptom screening and sputa collection (if the contact is able to cough and produce specimens) is recommended to “clear “ the contact and rule out active TB. Sometimes, contacts deny having a productive cough yet can produce adequate sputa specimens. Fully evaluating symptomatic contacts for TB disease in remote villages is challenging if not impossible due to the lack of skilled providers and x-ray capability in many small communities. Sputa collection, which would be included in a complete medical evaluation, can be done even in the most remote locations as long as specimens are sent to ASPHL as soon as possible after collection.

Figure 6: EVALUATION, TREATMENT, AND FOLLOW-UP OF CONTACTS WITH PRIOR POSITIVE TUBERCULIN SKIN TESTS[55]



Definition of abbreviations: HIV = human immunodeficiency virus; LTBI = latent tuberculosis infection.

* Before initiation of treatment, contacts should be evaluated fully for TB disease. A full course treatment is recommended for HIV-infected contacts in this category.

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: 20% 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, household contacts with a positive tuberculin skin test (TST) results are more likely to be infected recently (or as a result of exposure to the index patient) if the contacts are U.S.-born children rather than adults born in high-incidence countries.
   - **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 change in TST status from negative to positive

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.

Sometimes the result from an investigation indicates a need for expansion, but resources do not permit this. In these situations, seek consultation and assistance from the next higher level in public health administration (e.g., the county health department consults with the state health department). Consultation offers an objective review of

strategy and results, additional expertise, and the potential for personnel or funds for meeting needs.

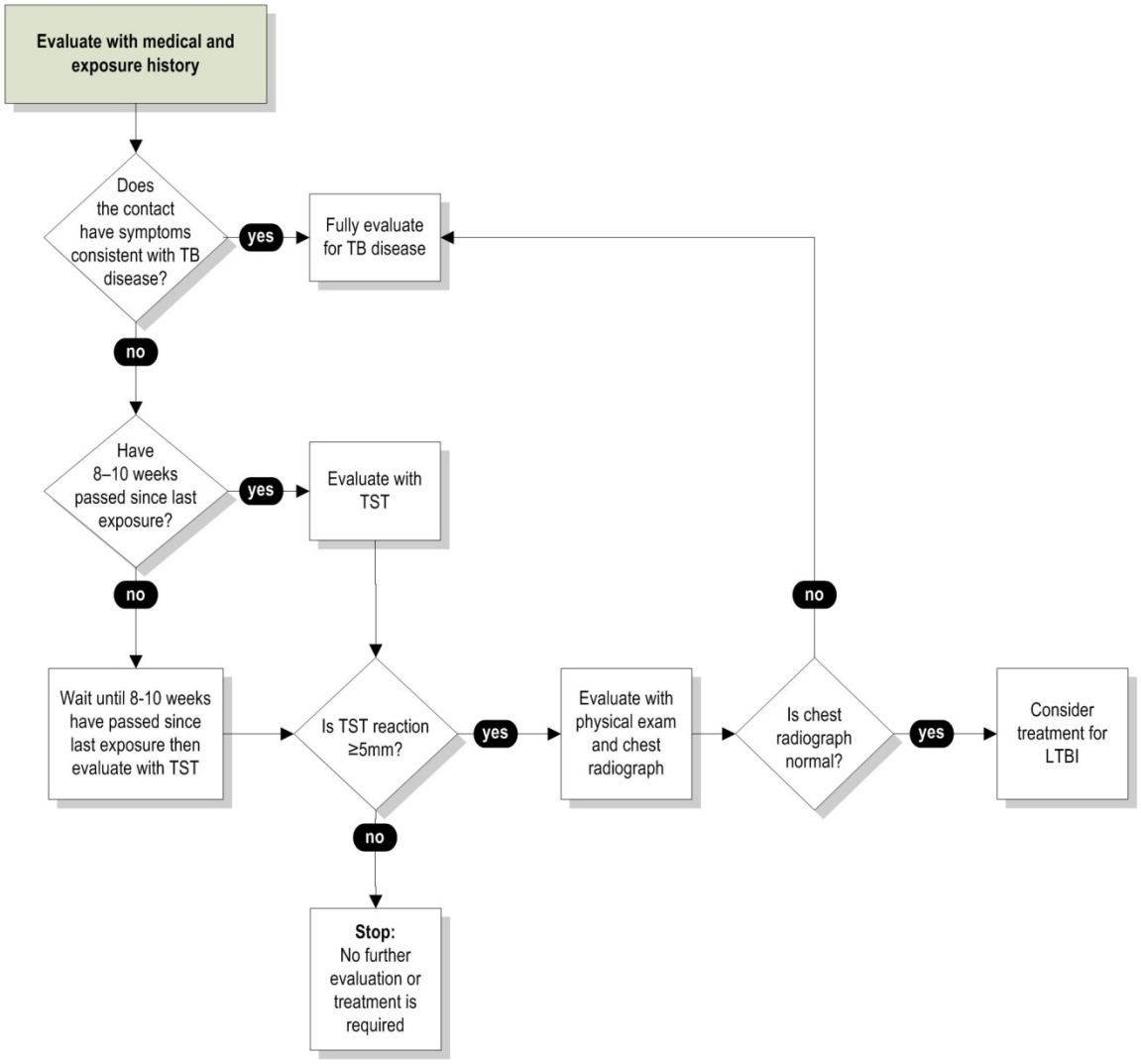
Contact the Alaska TB Program at 907-269-8000 to consult about expanding a contact investigation.

Low-Priority Contacts

Use Figure 7 to select evaluation, treatment, and follow-up activities for low-priority contacts.

Evaluate low-priority contacts with medical and exposure history. Based on these histories, take the actions in the Figure 7.

Figure 7: EVALUATION, TREATMENT, AND FOLLOW-UP OF LOW-PRIORITY CONTACTS[56]



Definition of abbreviations: CXR = chest radiograph; IGRA = interferon gamma release assay; LTBI = latent tuberculosis infection; 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):18.

Data Management and Evaluation of Contact Investigations

Data collection related to contact investigations 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 and overall 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 are 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 tuberculin skin test (TST) administered to a contact).

Completion of Investigation

When aggregated, the data from an investigation inform public health officials as to whether the investigation is on time and complete. 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 the 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, then the reasons for problems can be studied.

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 , is recommended for assessing the overall activities of contact investigations.

Index Patient and Contact Data

Use the *TB Case Management Form* to collect the data on each index patient and the *Contact Investigation Form* to collect the data on individual contacts. Both are available in the Forms section of this manual **18.1**.

Table 7: DATA ABOUT THE INDEX PATIENT[57]

Identifiers/Demographic Information	Case manager Name and aliases For minors and dependents: guardian information Date of birth 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) Alcohol and 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 cavity TB medications with start and stop dates Bacteriologic results (sputum smear, NAA, 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 8: DATA ABOUT EACH CONTACT[58]

Investigator and Dates	Dates of interviews Start and end dates for exposure (updated as new information arrives)
Identifiers	Name and aliases For minors and dependents: guardian information Date of birth 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., 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 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) Adverse reactions (specify each) Interruptions in regimen and dates Outcome of treatment (completion, etc., consistent with *ARPE*†) If treatment not completed, reason†

Definitions of abbreviations: *ARPE* = *Aggregate Report for Program Evaluation*; 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.

† As defined by CDC *ARPE* for contact investigations.

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, were tested, started therapy, and completed therapy.

Record your summary on the *Contact Investigation Form* available in the Forms section of this manual **18.1**.

In addition, the CDC's Framework for Program Evaluation in Public Health is recommended for assessing the overall activities of contact investigations.[59]

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 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:

Criteria based on surveillance and epidemiology:

1. An increase has occurred 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 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:

Transmission is continuing despite adequate control efforts by the TB control program

Contact investigation associated with increased cases requires additional outside help

Deoxyribonucleic Acid Genotyping

Deoxyribonucleic acid (DNA) genotyping is routinely done on all Alaska TB isolates at a regional genotyping laboratory. It is also a laboratory technique used by public health officials to distinguish between different strains of *M. tuberculosis* and to help assess the

likelihood of TB transmission. Characterization of *M. tuberculosis* with DNA genotyping is a powerful tool for the following:

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 infections
4. Identifying laboratory cross-contamination as the cause of misdiagnosis

For more information regarding Deoxyribonucleic Acid Genotyping, refer to the National TB Controllers Association/CDC Advisory Group on Tuberculosis Genotyping. *Guide to the Application of Genotyping to Tuberculosis and Control.* Atlanta, GA: US department of Health and Human Services, CDC: June 2004. Available at: https://www.cdc.gov/tb/programs/genotyping/images/tbgenotypingguide_june2004.pdf

Resources and References

Resources

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[59] 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):22.

Laboratory Services

CONTENTS

Introduction

Purpose

Use this section to

- get contact information for laboratories;
- determine which tests are available and the tests' turnaround times; and
- identify which laboratory can perform 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]

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

State Laws and Regulations

Laboratories must report *Mycobacterium tuberculosis.* Alaska Statutes and Regulations pertaining to the control of tuberculosis in Alaska are available in the Statutes and Regulations section of the manual **19.1**.

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 • Receives and performs primary specimen AFB concentrated smear and culture testing for mycobacteria • Susceptibility testing of first-line drugs on *Mycobacterium tuberculosis* complex isolates	Alaska State Public Health Laboratory (ASPHL) Mycobacteriology Laboratory 5455 Martin Luther King Jr Ave. P.O. Box 196093 Anchorage, AK 99507 Tel: (907) 334-2100 Fax: (907) 334-2161
Private Laboratories • Non-tuberculosis *mycobacterium* susceptibility testing • Confirmation of first-line drug testing on *Mycobacterium tuberculosis* complex isolates • Second-line drug testing on *Mycobacterium tuberculosis* complex isolates	National Jewish Health Mycobacteriology Reference Laboratory 1400 Jackson St. Denver, CO 80206 Tel: (303) 398-1339 Fax: (303) 398-1953

Available Laboratory Tests

Table 2: LABORATORY TESTS AVAILABLE IN ALASKA

Test	Laboratory	Turnaround Time
Diagnosis		
Acid-fast bacilli (AFB) smear (fluorochrome)	Alaska State Public Health Laboratory	Within 24 hours from receipt of specimen in the laboratory Monday thru Friday only (closed on national holidays)
Culture	Alaska State Public Health Laboratory	Cultures are incubated for 6 weeks before reported as negative. Time to detection of Mycobacterial growth is dependent upon growth rate and quality of specimen. Identification of cultured mycobacteria is usually within 14-21 days from date of receipt (this can be dependent on factors such as overgrowth by other organisms).
Drug susceptibility (first-line drugs only)	Alaska State Public Health Laboratory	Within 15 days from identification
Nucleic acid amplification (NAA) test Please see NAAT section 12.5	Alaska State Public Health Laboratory	GeneXpert® Xpert® MTB/RIF Assay: within 24 hours from receipt of specimen in the laboratory. TB PCR: within 24 – 72 hours from receipt of specimen in the laboratory (performed Monday, Wednesday and Friday)
QuantiFERON®-TB Gold In-Tube (QFT-GIT)	Testing is only available at private reference labs in Alaska	Varies with laboratory
Epidemiologic Monitoring		
Genotyping*	Michigan Department of Community Health – TB Lab 927 Terminal Rd. Lansing, MI 48906 Tel: (517) 335-8395	Within 14 days of receipt of *Mycobacterium tuberculosis* complex isolates

* All isolates of *M. tuberculosis* identified at the ASPHL are sent to the Michigan Department of Community Health Laboratory for genotyping. On the rare occasion that M. *tuberculosis* is identified at another laboratory, arrangements must be made for isolates to be sent to the ASPHL so that genotyping can be done.

Laboratories should report positive smears, NAA or positive cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the health department, as specified in the "Reporting Tuberculosis" topic in the Surveillance section **(2.6)**. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[4]

For information on reporting, see the "Reporting Tuberculosis" topic in the Surveillance section **2.6**.

For laboratory services available in Alaska, contact the Mycobacteriology Department at 907-334-2139.

TB Nucleic Acid Amplification Testing (NAAT):

The ASPHL will perform the Xpert® MTB/RIF Assay on **initial smear-positive sputum specimens**. Additionally, ASPHL will perform the Xpert® MTB/RIF Assay on **smear-negative sputum specimens** from patients considered to be TB suspects upon provider request and **pre-approval** from the Alaska Tuberculosis Program. Non-sputum samples and samples from patients younger than 18 will be tested using the ASPHL in-house TB PCR assay. The *TB NAA Testing Authorization Form* must be completed prior to testing.

Patient Criteria

- Patient must have signs and symptoms of pulmonary TB
- Patient must be reported to the Alaska Tuberculosis Program as a TB suspect or TB case (907-269-8000)
- Patient must not have been diagnosed with TB or a nontuberculous mycobacterial infection or received treatment within the last 12 months

The link to the most current version of the *TB NAA Testing Authorization Form* is available in the Forms Section of the Manual **18.1.**

Refer to Tables 3, 4 & 5: **NAA Testing Algorithm and Result Interpretation** for information about interpreting the results.

Table 3: GENEXPERT® XPERT® MTB/RIF ASSAY RESULT INTERPRETATION

Smear Result	MTB/RIF Assay Result	Interpretation
Smear Positive for AFB	MTB DETECTED	MTB target is detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAA test does not necessarily indicate the presence of viable organisms.
	MTB Not Detected	MTB target is not detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A patient is presumed to have an infection with nontuberculous mycobacteria, pending culture results. A negative MTB result on the Xpert MTB/RIF assay does not rule out pulmonary TB.
Smear Negative for AFB	MTB DETECTED	MTB target is detected within the sample. Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAA test does not necessarily indicate the presence of viable organisms.
	MTB Not Detected	Use clinical judgment to determine whether to begin therapy while awaiting results of culture and other diagnostic tests. A negative MTB result on the Xpert MTB/RIF assay does not rule out pulmonary TB.

Table 4: GENEXPERT® XPERT® RIFAMPIN RESULT INTERPRETATION

Rifampin Result	Interpretation
RIF Resistance NOT DETECTED	No *rpoB* mutation detected; likely rifampin susceptible.
RIF Resistance DETECTED	*rpoB* mutation detected; likely rifampin resistant. Confirmatory testing in progress.
RIF Resistance INDETERMINATE	Insufficient MTB in the sample to allow determination of the *rpoB* mutation result.

Table 5: ASPHL TB PCR RESULT INTERPRETATION

Smear Result	TB PCR Result	Interpretation
Smear Positive for AFB	DNA DETECTED	Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAA test does not necessarily indicate the presence of viable organisms.
	DNA Not Detected	Use clinical judgment to determine whether to begin therapy while awaiting culture results. A patient is presumed to have an infection with nontuberculous mycobacteria, pending culture results. A negative TB PCR result does not rule out TB.
Smear Negative for AFB	DNA DETECTED	Use clinical judgment to determine whether to begin therapy while awaiting culture results. A positive NAA test does not necessarily indicate the presence of viable organisms.
	DNA Not detected	Use clinical judgement to determine whether to begin therapy while awaiting results of culture and other diagnostic tests. A negative TB PCR result does not rule out TB.

Refer to Table 3: **PCR Testing Algorithm and Result Interpretation** for information about interpreting the results of PCR (NAA Testing).

Table 3: PCR Testing Algorithm and Result Interpretation

Smear Result	TB PCR Result	Interpretation
Smear Positive for AFB	*Mycobacterium tuberculosis* complex DNA detected	Presumed TB, pending culture results
	No *Mycobacterium tuberculosis* complex DNA detected	Use clinical judgment to determine whether to begin therapy while awaiting culture results. A patient is presumed to have an infection with non-tuberculosis mycobacteria, pending culture results.
Smear Negative for AFB	*Mycobacterium tuberculosis* complex DNA detected	Use clinical judgment to determine whether to begin therapy while awaiting results of culture and other diagnostic tests. Currently available PCR tests are not sufficiently sensitive to exclude the diagnosis of TB.
	No *Mycobacterium tuberculosis* complex DNA detected	Use clinical judgment to determine whether to begin therapy while awaiting results of culture and other diagnostic tests. Currently available PCR tests are not sufficiently sensitive to exclude the diagnosis of TB.

Specimen Collection

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, so 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 that inhibit the growth of contaminating organisms, since most specimens will contain bacteria other than mycobacteria.[5]

Refer to Table 4 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 .

Detailed information about diagnostic testing available at the Alaska State Public Health Laboratory (ASPHL) is available in the "Laboratory Services Manual". It is available at: http://dhss.alaska.gov/dph/Labs/Documents/LaboratoryTests.pdf

Highlights include:

- "Tuberculosis/Mycobacterium Detailed Collection Instructions" (for the provider and laboratorian) and "Instructions for Collecting Sputum Samples" (for the patient).
- A linked table of contents so you can click on the test of interest in the table of contents and it will take you directly to that page.
- General information about who can request testing, and how to obtain supplies, request forms, and shipping boxes.
- Tests are listed alphabetically and include specific information about the sample required, storage and transport recommended, and when you can expect results back.

The ASPHL website also contains contact information, explanations of the services offered, and the forms needed to request testing and supplies. It is available at: http://dhss.alaska.gov/dph/Labs/Documents/LaboratoryTests.pdf

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 (Submit in sterile 50 mL conical tube with 50 mg of sodium carbonate preservative)
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 (Submit in sterile 50 mL conical tube with 50 mg of sodium carbonate preservative)
Gastric aspirates can be submitted for the diagnosis of pulmonary tuberculosis (TB) in young children who cannot produce sputum.	▪ 5-10 ml of gastric contents (Adjust to neutral pH with 100 mg of sodium carbonate immediately following collection)
Bronchoscopy can be used in the following situations: ▪ If a patient cannot produce sputum by the above three methods[6] or ▪ If a patient has a substantial risk of drug-resistant TB and has initial routine studies that are negative[7] or ▪ In a patient in whom there is suspicion of endobroncheal TB[8] 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 ▪ Pleural ▪ Bone/joint ▪ Kidney ▪ Peritoneal ▪ Pericardial	Examples of fluids ▪ Pleural ▪ Cerebrospinal ▪ Blood ▪ Urine ▪ Synovial ▪ Peritoneal ▪ Pericardial
* Do not place specimens in formalin.		

How to Perform Spontaneous Sputum Collection at a Healthcare Facility

1. Collect the specimen in a specialized room or booth designed for cough-inducing procedures.
2. Instruct the patient on how to collect the sputum sample.
   a. 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.)
   b. Review with the patient how to collect sputum.
3. Make sure the specimen container and laboratory requisition are filled out completely before shipping.
   a. On the specimen container, record the patient name and the date and time of collection.
   b. Complete Test Request Form. These are located on the ASPHL website: http://dhss.alaska.gov/dph/Labs/Pages/publications/default.aspx
4. Make sure the specimen and laboratory requisition are packaged into appropriate shipping containers, per laboratory instructions.

Refer to the “Specimen Collection and Shipment Supplies” topic in the Supplies, Materials, and Services section, and see the “Specimen Shipment topic,” which follows.

5. 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.
6. Unless shipping by express delivery, such as Gold Streak, do not keep specimens to send all three on the same day.
7. Use the most rapid transport to the laboratory: You, courier, overnight carrier, or WE mail.

Make every effort to submit specimens to the laboratory within 24 hours of collection. Normal flora can overgrow any mycobacteria in the specimen and make it unusable. If specimens cannot be submitted within 24 hours, keep in mind that ASPHL will not run a specimen over 10 days old. Know how long it takes the specimen to get to the laboratory from the time it leaves your hands, and submit specimens accordingly.

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 (5 to 10 ml is an adequate amount).
2. Review with the patient how to collect sputum.
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.

Induced Sputum Collection at a Healthcare Facility

If the patient cannot produce sputum spontaneously, then make arrangements for induced sputum to be collected at a facility. Facilities where sputum can be collected include the respiratory therapy department of a local hospital or TB clinic. Facilities should have appropriate respiratory protection, environmental controls, and policies and procedures.

How to Collect Gastric Aspirates

The following are basic guidelines for collecting gastric aspirates:

- Collect the specimen after the patient has fasted for 8 to 10 hours and, preferably, while the patient is still in bed.
- Put sample into 50 mL conical tube with 100 mg of sodium carbonate preservative.
- Collect a specimen daily for three days.

For additional information on how to collect a gastric aspirate and prepare the specimen for transport, see the guide and Francis J. Curry International Tuberculosis Center's online video *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure* at http://www.currytbcenter.ucsf.edu/topics-interest/pediatric-tb .

Bronchoscopy or Collection of Extrapulmonary Specimens

Physicians who plan to collect (extrapulmonary) specimens should send part of the specimen (not in formalin) to the microbiology laboratory to be forwarded to the ASPHL for acid-fast bacilli (AFB) smear and culture, in addition to any other tests or pathology examinations the physician plans to obtain. A post-bronchoscopy sputum specimen should be sent for AFB smear and culture.

- **Bronchoscopy:** Refer the patient to a local specialist.
- **Extrapulmonary specimens:** These specimens will be collected by the physician performing the diagnostic work-up.

Specimen Shipment

There are three main categories of transportation methods: medical couriers, ground transportation, and air transportation. Category B Infectious Substances (raw diagnostic specimens, such as sputum, blood, or tissue) can be mailed through the US Postal Service (USPS), air shipped by private carrier (e.g., Federal Express, Airborne Express, Gold Streak, etc.), or transported by a medical courier. Specimens collected for AFB smear and culture are Category B Infectious Substances (raw diagnostic specimens, such as sputum, blood, or tissue) and should be labeled and shipped as such.

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 by the 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 171–180 (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[9]

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.[10]

Specimens must be shipped according to current federal, state and local laws. Upon request, Alaska State Public Health Laboratory provides ambient temperature shipping boxes that meet current shipping regulations.

Refer to the shipping regulations that are listed under “Resources and References” at the end of this section. Personnel who handle, package, and ship infectious materials must be trained in these procedures.

For more information, contact ASPHL Lab at 907-334-2100. To request lab supplies, visit the website: http://dhss.alaska.gov/dph/Labs/Pages/publications/default.aspx

Use the *Anchorage Public Health Laboratory Request Form* to request tuberculosis laboratory services from the Alaska State Public Health Laboratory in Anchorage. It is available in the Forms section of the manual **18.1**.

To obtain specimen collection and transport supplies, see the topic on "Specimen Collection and Shipment Supplies" in the Supplies, Materials, and Services section **16.1**.

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. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33. Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/cid_ciw694_full.pdf
- 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).
- Francis J. Curry International Tuberculosis Center. *Pediatric TB: A Guide to the Gastric Aspirate (GA) Procedure* (Francis J. Curry National Tuberculosis Center Web site). Available at: http://www.nationaltbcenter.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).
- National Tuberculosis Controllers Association—National Tuberculosis Nurse Consultant Coalition. *Tuberculosis Nursing: A Comprehensive Guide to Patient Care* (Atlanta, GA; 1997):39–42.

- 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/ .

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3 APHL, The Future of Tuberculosis Laboratory Services: A Framework for Integration/Collaboration/Leadership. 2004. Available at: https://stacks.cdc.gov/view/cdc/11399

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[5] ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

[6] Iseman, MD. *A Clinician's Guide to Tuberculosis, 2000.* 1st ed. Philadelphia, PA: Williams & Wilkins; 2000:135–136.

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[8] Iseman, MD. *A Clinician's Guide to Tuberculosis, 2000.* 1st ed. Philadelphia, PA: Williams & Wilkins; 2000:135–136.

[9] National Jewish Medical and Research Center. *How to Mail Specimens and Cultures to the National Jewish Mycobacteriology Laboratory.* Denver, CO; March 2005:2.

[10] National Jewish Medical and Research Center. *How to Mail Specimens and Cultures to the National Jewish Mycobacteriology Laboratory.* Denver, CO; March 2005:5–7.

Patient Education

CONTENTS

Introduction

Purpose

Use this section to

- determine what information to cover in education sessions;
- educate patients about tuberculosis (TB);
- educate patients about latent TB infection (LTBI); and
- 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]

Policy

Public Health Nurses are responsible for patient teaching regarding:

- tuberculosis transmission and control
- treatment
- common side-effects of medicines used to treat tuberculosis
- the importance of compliance with recommended therapy.

In addition, they provide information to other health-care providers, community organizations, and other institutions.

The Alaska TB Program provides consultation and resources for client education and information concerning tuberculosis infection and disease, transmission of tuberculosis,

treatment, common side-effects of medicines used to treat tuberculosis, and the importance of compliance with recommended therapy

For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction **1.18**.

General Guidelines

Table 1: GUIDELINES FOR THE EDUCATIONAL PROCESS

When Educating Tuberculosis Patients	
Do	**Don't**
▪ Find out what patients know and believe about tuberculosis (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) appointments, and monthly monitoring, educate the patient as needed on the topics that follow.

For more information on case management activities, see the Case Management section **10.1**.

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* (Francis J. Curry National Tuberculosis Center Web site; 2003) at http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-07 .

For information on country-specific TB epidemiology, common misperceptions, beliefs, attitudes, and stigmatizing practices related to TB and HIV/AIDS, general practices and cultural courtesies, translated educational materials available online, and references, refer to: https://sntc.medicine.ufl.edu/Files/Products/Intro.pdf

Country-specific guides can be found at: http://sntc.medicine.ufl.edu/Products.aspx

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/library.cfm?fa=download&resourceID=89928&appView=folder&print .

For medical interpreters and translators, refer to:

Pacific Interpreters –
(800) 311-1232
http://www.pacificinterpreters.com/

Language Line:
(800)-752-6096 option 2
http://www.languageline.com/

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. .
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 private 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.

For more information on TB education, DOT and treatment agreements, contact investigation, side effects and potential drug interactions, and adherence with the treatment regimen, see the Case Management section of the manual **10.1**.

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.

Isolation

If isolation is necessary, educate the patient about how to take proper precautions.

1. Explain isolation precautions and restrictions, if appropriate.

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.
6. Review other medications, prescription and over the counter, the patient is taking to identify potential drug interactions.

For more information on side effects and adverse reactions, see the "Side Effects and Adverse Reactions" topic in the Treatment of Tuberculosis Disease section **6.9** or the Treatment of Latent Tuberculosis Infection section **8.10**.

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.
4. Use incentives and enablers to ensure adherence to the treatment regimen.

Patient Education Materials

Get the Facts About TB Disease
http://www.cdc.gov/tb/publications/pamphlets/TB_disease_EN_rev.pdf

- *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 2009* http://www.cdc.gov/tb/publications/faqs/pdfs/qa.pdf
- *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/tb.pdf
- *Tuberculosis: Get the Facts!* http://www.cdc.gov/tb/publications/pamphlets/TBgtfctsEng.pdf
- *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, consult the resources at the end of this section.

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; 2008). 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/pdfs/9.pdf .
  - Module 4: “Treatment of LatentTuberculosis Infection and Tuberculosis Disease, ” Available at: http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf
  - CDC. *TB Elimination: Now Is the Time!* (Division of Tuberculosis Elimination Web site;). Available at: http://www.cdc.gov/tb/publications/pamphlets/nowisthetime/pdfs/nowisthetime.pdf

  .

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/?404;http://www.cdc.gov:80/tb/pubs/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 .

References

[1] CDC. Module 4: treatment of Latent Tuberculosis Infection and Tuberculosis Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2016. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf . Accessed January 18, 2017.

[2] CDC. Module 4: treatment of Latent Tuberculosis Infection and Tuberculosis Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2016. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module04.pdf . Accessed January 18, 2017.

[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/pdfs/9.pdf . Accessed April 11, 2011.

Confidentiality

CONTENTS

Introduction

Purpose

Use this section to

- 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

The State of Alaska has adopted a Health Insurance Portability and Accountability Act (HIPAA) policy that conforms to the national act. Information regarding Alaska DHSS HIPAA may be found at http://dhss.alaska.gov/dhcs/Pages/hipaa/default.aspx

Healthcare workers should keep patient information in confidence and divulge it only with the permission of the patient, except as otherwise required by law.[2]

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

State Laws and Regulations

Alaska regulations pertaining to patient confidentiality may be found in the Statutes and Regulations section of the manual **19.1**.

Health Insurance Portability and Accountability Act (HIPAA)

Confidentiality of patient information is a requirement in the healthcare field and has its own set of regulations, the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The 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 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]

ALASKA HIPAA Policies

The Alaska Department of Health and Social Services is a covered entity. Alaska HIPPA policies may be found at

http://dhss.alaska.gov/dhcs/Pages/hipaa/default.aspx

http://www.epi.hss.state.ak.us/bulletins/docs/rr2003_02.pdf

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. ▪ 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.
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 Media	▪ Maintain confidentiality in communications with the media.

Resources and References

Resources

- CDC. “HIPAA Privacy Rule and Public Health: Guidance from CDC and the US Department of Health and Human Services” (*MMWR* 2003;52[S-2]). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/su5201a1.htm .
- CDC. Module 7: “Patient Rights and Confidentiality in Tuberculosis Control” (*Self-Study Modules on Tuberculosis.* Division of Tuberculosis Elimination Web site; 2011). Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/module7.pdf .
- United States Department of Health and Human Services. “Health Insurance Portability and Accountability Act of 1996.” (Public Law 104-191 Web site). Available at: https://aspe.hhs.gov/report/health-insurance-portability-and-accountability-act-1996.
- United States Department of Health and Human Services. “Office for Civil Rights—HIPAA” [Office for Civil Rights Web site]. Available at: http://www.hhs.gov/ocr/hipaa/ .

References

[1] CDC. Module 7: “ Patient Rights and Confidentiality in Tuberculosis Control. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2011. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/module7.pdf Accessed: January 10, 2017.

[2] CDC. Module 7: “ Patient Rights and Confidentiality in Tuberculosis Control. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2011. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/module7.pdf Accessed: January 10, 2017.

[3] CDC. HIPAA privacy rule and public health: guidance from CDC and the US Department of Health and Human Services. *MMWR* 2003;52(S-2):1.

Transfer Notifications

CONTENTS

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 U.S. 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 *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 Alaska TB Program is responsible for coordination of transfer notifications between states and other local jurisdictions within the state. The local public health jurisdiction should notify the Alaska TB Program 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.

For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction **1.18**.

Program Standards

The Alaska TB Program works with other jurisdictions to transfer information regarding persons receiving treatment for active TB, LTBI or persons who are contacts to TB cases. Local PHNs should work through the Alaska TB Program to facilitate all transfers.

When to Initiate a Notification

For a definition of tuberculosis (TB) patient classifications, see the "Tuberculosis Classification System" topic in the Diagnosis of Tuberculosis Disease section.

Table 1: TRANSFER NOTIFICATIONS AND FOLLOW-UPS[2]

Referral Type	When to Initiate	Notes
Verified and suspected cases of tuberculosis (TB) disease	When notified that a patient with active or suspect TB 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 or medium-priority contact to a smear-positive pulmonary case ▪ Contact to a smear-negative pulmonary case ▪ Contact to a highly suspect pulmonary case	Send individual referrals for each contact. Contacts to smear-negative cases and suspect TB cases may be low priorities for investigation by the receiving jurisdiction.
Latent TB Infection (LTBI)	When notified that a documented convertor who has initiated treatment is moving or has moved from the area for 30 days or more	Newly infected contacts to smear-positive cases are priorities for LTBI treatment.
Source case investigation for TB disease	After identifying a close associate to an active 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]
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 Recommendations2014-2015*

How to Issue a Notification

How a notification is made depends upon whether the transfer occurred:

- Inside the United States
- Outside the United States

Transfers Inside the United States

The Alaska TB program will assist with transfers of patients within the state of Alaska.

Refer to Table 2: **Transfers Within Alaska**

Transfers Between States: 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] Refer to

Table 2: **Referrals in the United States.**

The Alaska TB Program will take the following steps to send a referral to notify another jurisdiction to which a patient has moved or another jurisdiction in which a contact/associate is identified.

Table 2: REFERRALS IN THE UNITED STATES[6]

Action	Transfers Within Alaska	Transfers Between States
Make a referral	The public health agency from which the patient is transferring should do the following as soon as possible: ▪ Call the Alaska TB Program at 907-269-8000 ▪ Copy the updated, complete local public health file on the patient, and send the copy to the jurisdiction receiving the patient ▪ Call the patient's private 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 public health agency from which the patient is transferring should do the following as soon as possible: ▪ Call the Alaska Tuberculosis Program at 907-269-8000 ▪ Fill out the NTCA's "Interjurisdictional TB Notification (IJN)" form* ▪ Mail and fax the form to the Alaska Tuberculosis Program l at • Mail: 3601 C St, etc. • Fax: 907-563-7868 If more information is needed, the Alaska TB Program will request it from the public health agency from which the patient is transferring

Action	Transfers Within Alaska	Transfers Between States
Provide records to patient	The public health agency from which the patient is transferring should provide the patient a copy of the treatment records	The public health agency from which the patient is transferring should provide the patient a copy of the referral and treatment records
Send the referral form	Not necessary	Use the NTCA's "Interjurisdictional TB Notification Follow-Up" form†

* The NTCA's "Interjurisdictional Tuberculosis Notification" form is available online at http://www.tbcontrollers.org/docs/resources/IJN_Form_May2015.pdf

† NTCA's "Interjurisdictional TB Notification Follow-Up" form is available online at http://www.tbcontrollers.org/docs/resources/IJN_FollowUpForm_November2014.pdf

The Alaska TB Program usually works with PHNs in Alaska and completes the *Interjurisdictional Tuberculosis (TB) Notification* and *Interjurisdictional Tuberculosis (TB)* Notification *Follow-up* forms to assist with the transfer.

http://www.tbcontrollers.org/docs/resources/IJN_Form_May2015.pdf

http://www.tbcontrollers.org/docs/resources/IJN_FollowUpForm_November2014.pdf

For more information on completing the NTCA forms, see the NTCA's *Interjurisdictional Tuberculosis (TB) Notification—National Tuberculosis Controllers Association Recommendations* (NTCA Web site) at:

http://www.tbcontrollers.org/resources/interjurisdictional-transfers/#.WGboB00zWmx

Transfers Outside the United States

Centers for Disease Control and Prevention International Notifications

The Alaska TB Program is responsible for international transfer notifications. The local health jurisdiction should notify the state health department when a patient moves outside the country.

Local healthcare agency staff: The information below is provided for your information only. Alaska TB Program staff will fill out these forms.

A process for international notification of TB cases has been developed by the CDC to provide information to TB control staff in the country of the patient's destination.[7] The CDC notification process covers the following regions:

- African Region
- Americas Region
- Eastern Mediterranean Region
- European Region
- Southeast Asia Region
- Western Pacific and East Asia Region

In Alaska, send these referrals directly to the Alaska TB Program as soon as possible after receiving information about the patient's move or identifying a contact/associate.

To make an international referral through CDC:

1. Complete the International Tuberculosis Notification Form http://www.cdc.gov/tb/programs/international/PDF/internat_proces.pdf
2. Forward a copy of the notification by fax to the Alaska TB Program.
3. The Alaska Tuberculosis Program will forward the referral to CDC.

   For contact information, see the CDC Website at http://www.cdc.gov/tb/programs/international/PDF/NTPcontactinfoWHO.pdf

Provide the patient with

a. A copy of the referral and treatment records.

Transition doses of medications will be provided on a case-by-case basis by the Alaska TB Program

CURE-TB: Transfers to Mexico

In addition to the CDC notification, The Alaska TB Program will make referrals through CURE-TB (http://www.curetb.org), a referral program for TB patients and their contacts moving between the U.S. and Mexico. This program provides direct guidance to patients and facilitates the exchange of information between providers in both countries. Services are available to patients and providers all over the U.S. and Mexico.[8]

Referrals accepted by the CURE-TB program include the following:

- **Patients** with suspected or confirmed TB disease who are moving or spending more than one month in Mexico
- **Contacts who move** between the U.S. and Mexico
- **Contacts living in Mexico** who have been exposed to a confirmed case living in the U.S.
- **Source case finding** for an index case in the U.S. when there is reasonable suspicion of TB disease in a person living in Mexico
- **Requests for a patient's clinical history** while living in Mexico, if sufficient locating information regarding the Mexican provider is supplied

To initiate a CURE-TB referral:

1. Complete the CURE-TB Referral Form http://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/documents/CureTB_Binational_Notification_Form.pdf
2. Forward a copy of the referral form by fax to the Alaska TB Program
   a. The CURE-TB fax number is 1-619-692-8020. CURE-TB can be reached by telephone at 1-619-542-4013

3. Provide the patient with

   a. the CURE-TB telephone numbers to call (1-800-789-1751 in the U.S.; 001-800-789-1751 in Mexico) for questions about their care or about accessing care on either side of the border;[9]

   b. a copy of the referral and treatment records;

Medications will be provided on a case-by-case basis by the Alaska TB Program

TBNet: International Transfers in Mobile, Underserved Populations

TBNet (http://www.migrantclinician.org/network/tbnet) is a multinational TB patient tracking and referral project for mobile, underserved populations. Although the program was originally created for migrant farm workers, it is expanding to include any patient who might be mobile during their treatment, such as the homeless, immigration detainees, or prison parolees.[10]

TBNet offers the following services:

- **Portable, wallet-sized treatment records.** TBNet supplies TB clinics with records that summarize a patient's TB treatment and can easily be carried by the patient.
- **Toll-free line (1-800-825-8205) for healthcare providers and patients.** Healthcare providers from the U.S. or Mexico can call to request an up-to-date copy of medical records of patients enrolled in TBNet. Patients can call for help with locating treatment facilities at their next destination.

The Alaska TB Program initiates a TBNet referral within 30 days of the start of treatment.

To enroll a patient in TBNet:

1. Call TBNet Program Manager, at 1-800-825-8205 to begin the referral process.
2. Complete the TBNet Patient History and Brief Medical Information Form. http://www.migrantclinician.org/files/resourcebox/TBNet_Pt_History___Med_Info.pdf
3. Fax the form and copies of the chest radiograph and all laboratory reports to TBNet at 1-512-327-6140.[11]
4. Provide the patient with the portable, wallet-sized treatment record and TBNet's toll free number (1-800-825-8205).

References

[1] CDC. International notification of tuberculosis cases [Division of Tuberculosis Elimination Web site]. Available at: http://www.cdc.gov/tb/programs/international/default.htm . Accessed April 11, 2011.

[2] NTCA. *Interjurisdictional Tuberculosis (TB) Notification—National Tuberculosis Controllers Association Recommendations* [NTCA Web site]. March 2002:1–5. Available at: http://tbcontrollers.org/docs/IJ_Form_Page1.pdf . Accessed January 11, 2017.

[3] 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):31.

[4] 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):31.

[5] NTCA. *Interjurisdictional Tuberculosis (TB) Notification—National Tuberculosis Controllers Association Recommendations* [NTCA Web site]. March 2002:1–5. Available at: http://tbcontrollers.org/docs/IJ_Form_Page1.pdf . Accessed January 11, 2017.

[6] NTCA. *Interjurisdictional Tuberculosis (TB) Notification—National Tuberculosis Controllers Association Recommendations* [NTCA Web site]. March 2002:1–5. Available at: http://tbcontrollers.org/docs/IJ_Form_Page1.pdf . Accessed January 11, 2017.

SUPPLIES AND SERVICES PROVIDED BY THE ALASKA TUBERCULOSIS PROGRAM

Item	Who May Order/Use	Cost to Patient	How to Obtain	Contact
Pharmaceuticals				
Purified Protein Derivative (PPD)	PHNs and Public Health Centers Schools	No cost	Fax *PPD Order Form* (18.1) to Epi Drug Room ONLY AVAILABLE TO PHNS AND FOR IN-SCHOOL TB TESTING	SOE Drug Room 907-341-2207 (f) 907-341-2228
TB Medications*	PHNs (Health care providers order through PHNs)	No cost	Fax *TB/LTBI Medication Request* (18.1) to the AK TB Program	AK TB Program 907-269-8000 (f) 907-563-7868
Pill crushers	PHNs	No cost	Indicate "pill crusher" on *TB/LTBI Medication Request* (18.1)	AK TB Program 907-269-8000 (f) 907-563-7868
Lab Supplies				
Sputum collection containers and packaging materials	Health care providers	No cost	Fax *ASPHL Supply Request Form* (18.1) to ASPHL- Anchorage	ASPHL-Anchorage 907-334-2100 (f) 907-334-2161
Other Supplies				
TB Screening and Clearance cards	Health care providers	No cost	Call AK TB Program	AK TB Program 907-269-8000 (f) 907-563-7868
Incentives and Enablers†	PHNs only	No cost	Contact Regional Nurse Manager	
Services				
Chest Radiograph (CXR) Single view± (CPT 71010)	Health care providers caring for non-insured/underinsured patients outside of Anchorage	AK TB Program reimburses up to $125 per CXR	Call an Epi Nurse for a CXR authorization number. Use the *Referral and Authorization for TB Screening and Follow-up Services (18.1)*.	AK TB Program 907-269-8000 (f) 907-563-7868
CXR interpretation	As above	No cost	Automatic on any submitted CXR. Use the *Tuberculosis Screening Questionnaire /CXR Interpretation Request* (18.1).	AK TB Program 907-269-8000 (f) 907-563-7868
Liver Function Tests –AST, ALT, bilirubin (CPT 80076) Venipuncture (CPT 36415)	Health care providers caring for non-insured/underinsured patients outside of Anchorage	Reimbursement up to $110 for LFTs and up to $40 for venipuncture	Call an Epi Nurse for a LFT authorization number. Use the *Referral and Authorization for TB Screening and Follow-up Services (18.1).*	AK TB Program 907-269-8000 (f) 907-563-7868
Medical Consultations±	Health care providers	No cost	Call AK TB Program	AK TB Program 907-269-8000 (f) 907-563-7868
IGRA testing	Health care providers	AK TB Program does not provide/ reimburse	Limited availability through private providers and labs in Alaska	

*All providers prescribing and /or requesting medications from the SOE Drug Room agree to use standard and approved regimens as referenced in this AK TB Manual to treat individuals for suspected or confirmed tuberculosis or LTBI. In special situations and after consultation with the Alaska TB Program, other regimens may be approved if clinically indicated.

†When funding is available.

±The Municipality of Anchorage provides TB clinical services, CXRs, and medical consultations within the Municipality of Anchorage, 825 L Street, Anchorage, AK 99501. Call 907-343-4799 to obtain these services.

Infection Control

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska guidelines to

- review the hierarchy of infection control measures and know where to go for further information;
- alert local public health staff to the basic differences between masks and respirators;
- estimate patients' infectiousness and determine when patients are noninfectious;
- determine when to isolate patients, when to discharge them from hospitals, and when to permit them to return to work, school, or other settings;
- review how to implement infection control measures in residential settings, patient care facilities, and transportation vehicles;
- consult with facilities that are implementing infection control measures, including two-step testing.

In the 2005 guidelines, "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 tuberculosis (TB) morbidity and mortality is the identification of settings in which a high risk exists for transmission of *Mycobacterium tuberculosis* and application of effective infection control measures.[1]

As TB continues to decline in most areas of the U.S., it is crucial that state and local public health agencies provide facilities with epidemiological data on TB, as well as education and guidance in developing effective TB infection control programs.

Infection control measures are fundamental to reducing the spread of communicable diseases such as TB. Transmission of *M. tuberculosis f*rom person to person can occur in many locations, such as home, work, school, and healthcare facilities.[2] It is impossible to prevent all exposure; however, the goal is to reduce the amount of transmission.

Every healthcare setting should have a TB infection control plan that is part of an overall infection control program. Each agency's or facility's program should include a hierarchy of administrative controls, environmental controls, and personal respiratory protection. Because each patient care setting and patient's home is different, each program will incorporate a different combination of control activities. The extent to which each agency or facility implements its control activities is based on the results of its risk assessment. In areas where TB rates are lower, the TB risk is lower, and this should affect which elements of the TB infection control plan are utilized. This section provides an overview

of TB infection control principles and is not designed to replace specific infection control plans in health care facilities.

Policy

Three main areas of infection control that need to be addressed by state and local public healthcare agencies are TB control in

1. healthcare facilities, where persons with infectious TB disease would seek care;[3,4]
2. congregate settings and residential facilities, whose residents are at increased risk for TB disease;[5,6]
3. the patient's home.

To accomplish TB control activities, each local public healthcare agency should do the following:

1. Familiarize staff with the current Centers for Disease Control and Prevention (CDC) infection control guidelines for healthcare providers and settings.
2. Develop an infection control program for the county or state TB staff, focusing on
   a. assignment of responsibility for program;
   b. risk assessment;
   c. persons (if anyone) who need baseline testing, including TB screening and counseling;
   d. education and training;
   e. case management (if direct patient care is provided).
3. Designate a staff person to guide facilities that may need to set up TB infection control programs.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction **1.18**.

Hierarchy of Infection Control Measures

There are three types of infection control measures. The first are administrative controls, which are primarily aimed at early identification, isolation, and appropriate treatment of infectious patients. The second are environmental controls, which focus on preventing the spread and reducing the concentration of infectious droplet nuclei in the air.[7] The third is personal respiratory protection, which may provide additional protection for healthcare workers in high-risk settings such as isolation rooms and cough-inducing or aerosol-generating suites.

The activities described below are more relevant to infection control in healthcare or residential facilities. Home settings are discussed separately in the "Residential Settings" topic in this section.

Administrative Controls

Administrative control measures are the first of three levels of measures designed to reduce the risk of tuberculosis (TB) transmission. Administrative controls are the first level of infection control because they include a variety of activities to identify, isolate, and appropriately treat persons suspected of having TB disease.

An effective TB infection control plan contains measures for reducing the spread of TB that are appropriate to the risk of a particular setting.[8] Every healthcare setting should have a TB infection control plan that is part of an overall infection control program.[9] A written TB infection control plan helps to ensure prompt detection, airborne precautions, and treatment of persons who have suspected or confirmed TB disease.[10]

- **In TB infection control programs for settings in which patients with suspected or confirmed TB disease are expected to be encountered,** develop a written TB infection control plan that outlines a protocol for the prompt recognition and initiation of airborne precautions for persons with suspected or confirmed TB disease, and update it annually.[11]
- **In TB infection control program for settings in which patients with suspected or confirmed TB disease are NOT expected to be encountered,** develop a written TB infection control plan that outlines a protocol for the prompt recognition and transfer of persons who have suspected or confirmed TB disease to another healthcare setting. The plan should indicate procedures to follow to separate persons with suspected or confirmed infectious TB disease from other persons in the setting until the time of transfer. Evaluate the plan annually, if possible, to ensure that the setting remains one in which persons who have suspected or confirmed TB disease are not encountered, and that they are promptly transferred.[12]

Administrative Activities[13]

Key activities to reduce the risk of transmission include the following:

1. **Assign responsibility** to a specific person for designing, implementing, evaluating, and maintaining a TB infection control program for that facility.
2. **Conduct a risk assessment.** The risk level of a particular facility will affect the extent of all other activities and will result in each facility having a different plan.
3. **Develop, implement, and enforce policies and procedures** to ensure early identification, evaluation, and treatment of infectious cases of TB.
4. **Provide prompt triage** and management in the outpatient setting of patients who may have infectious TB.
5. **Initiate promptly and maintain TB isolation** for persons who may have infectious TB and are admitted to an inpatient setting.
6. **Plan effectively for the discharge** of the patient, coordinating between the local public health agency and the healthcare provider.
7. **Implement environmental controls.** Develop, install, maintain, and evaluate the effectiveness of engineering controls.
8. **Implement a respiratory protection program.** Develop, initiate, install, maintain, and evaluate the effectiveness of the respiratory protection program.
9. **Implement precautions for cough-inducing procedures.** Develop, implement, and enforce policies and procedures to ensure adequate precautions when performing cough-inducing procedures.
10. **Educate and train healthcare workers** about TB.
11. **Counsel and screen healthcare workers.** Develop and implement counseling and screening program for healthcare workers about TB disease and latent TB infection (LTBI).
12. **Evaluate promptly possible episodes of TB transmission.**
13. **Coordinate activities** between the state and local public healthcare agencies.

Environmental Controls

TB is caused by an organism called *Mycobacterium tuberculosis.* When a person with infectious TB disease coughs or sneezes, tiny particles called droplet nuclei that contain *M. tuberculosis* are expelled into the air.[14] Environmental controls are used to prevent the spread and reduce the concentration of infectious droplet nuclei.[15] Each facility should use different combinations of environmental controls, based on the results of its risk assessment.

It is important to note, however, that without strong administrative controls, environmental controls are ineffective because cases would not be recognized or managed appropriately.

Table 1 describes the three main types of environmental controls.

Table 1: THREE TYPES OF ENVIRONMENTAL CONTROLS

Most Effective Control	Ventilation ▪ Controls direction of air flow to prevent contamination of air in areas surrounding a person with infectious tuberculosis (TB) ▪ Dilutes and removes contaminated air ▪ Exhausts contaminated air to the outside
Supplementary Controls	High-efficiency particulate air (HEPA) filtration ▪ Cleans the air of infectious droplet nuclei Ultraviolet germicidal irradiation (UVGI) ▪ Kills or inactivates TB bacilli in the air

Personal Respiratory Protection

Although administrative controls and environmental controls are most effective in controlling the spread of TB, they do not eliminate the risk of transmission entirely. Personal respiratory protection, the third level of infection control, is also used in higher-risk settings.

The purpose of a respirator is to reduce exposure by filtering out TB bacilli from the room air before the air is breathed into a person's lungs. Respirators used for TB control should be approved for TB use by the National Institute for Occupational Safety and Health (NIOSH).

It is recommended that healthcare provider staff and visitors use personal respiratory protective equipment in settings that may be at higher risk for TB transmission, such as the following:

- Rooms where infectious TB patients are being isolated
- Areas where cough-inducing or aerosol-generating procedures are performed
- Other areas, which should be identified in the facility's risk assessment, where administrative and environmental controls are not likely to protect persons from inhaling infectious droplet nuclei

It is important to note that the precise level of effectiveness (of respiratory protection) in protecting healthcare workers from *M. tuberculosis* transmission in healthcare settings has not been determined.[16]

Surgical-type masks are to be used by persons who are infectious or are suspected cases of TB disease when they are out of TB respiratory isolation. The purpose of the mask is to reduce transmission by reducing the number of TB bacilli coughed out into the room air. The infectious patient should not wear a respirator. For more information, see Table 2: **Using Masks and Respirators.**

When TB respirators are used, a respiratory protection program should be developed and enforced.[1,17] For more information respiratory protection programs, see the Centers for Disease Control and Prevention's (CDC's) "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005" (*MMWR* 2005;54[No. RR-17]:75–79) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf .

The new CDC guidelines recommend that healthcare facilities conduct annual training regarding multiple topics for healthcare workers (HCWs), including the nature, extent, and hazards of TB disease in the healthcare setting. The training can be conducted in conjunction with other related training regarding infectious disease associated with airborne transmission.

In addition, training topics should include the following:

1. Risk assessment process and its relation to the respirator program, including signs and symbols used to indicate that respirators are required in certain areas and the reasons for using respirators
2. Environmental controls used to prevent the spread and reduce the concentration of infectious droplet nuclei
3. Selection of a particular respirator for a given hazard (See “Selection of Respirators” on p. 78 of the CDC guidelines.)
4. Operation, capabilities, and limitations of respirators
5. Cautions regarding facial hair and respirator use
6. Occupational Health and Safety Administration (OSHA) regulations regarding respirators, including assessment of employees' knowledge

Trainees should be provided opportunities to handle and wear a respirator until they become proficient. Trainees should also be provided with copies or summaries of lecture materials for use as references and instructions to refer all respirator problems immediately to the respiratory program administrator.[18]

A fit test is used to determine which respirator fits the user adequately and to ensure that the user knows when the respirator fits properly. Fit testing provides a means to determine which respirator model and size fits the wearer best and to confirm that the wearer can don the respirator properly to achieve a good fit. Periodic fit testing for respirators used in TB environments can serve as an effective training tool in conjunction with the content included in employee training and retraining.[19]

The CDC recommends that, after a risk assessment to validate the need for respiratory protection, a healthcare facility should perform fit testing during the initial respiratory protection program training and periodically thereafter in accordance with federal, state, and local regulations.[20] The frequency of periodic fit testing should be supplemented by the occurrence of 1) risk for transmission of *M. tuberculosis,* 2) facial features of the wearer, 3) medical condition that would affect respiratory function, 4) physical characteristics of respirator, or 5) model or size of the assigned respirator.[21]

The OSHA also developed its own TB Rule, although it was withdrawn in 2003. However, OSHA has addressed TB in their general respiratory protection requirements, which includes the need for the following:

- Respiratory protection program
- Amended medical evaluation
- Training and recordkeeping
- Annual fit testing
- Fit checking

For regulations in your area, refer to state and local regulations and contact your local OSHA office. A directory of OSHA offices may be found at http://www.osha.gov/oshdir/ak.html

Information about the Alaska State Plan is available at: http://www.osha.gov/dcsp/osp/stateprogs/alaska.html

Who Should Use a Mask or Respirator

Using masks and respirators properly can reduce transmission of *Mycobacterium tuberculosis* and exposure to TB. Refer to Table 2: **Using Masks and Respirators** to determine when to use masks and respirators.

Table 2: USING MASKS AND RESPIRATORS[22]

Mask (a regular "surgical" mask*)	Respirator (NIOSH-approved, N-95 or higher*)
Purpose To reduce transmission by capturing infectious droplet nuclei that an infectious patient releases before they get into the air.	Purpose To reduce exposure by filtering infectious droplet nuclei out of the air, before the wearer breathes the air into their lungs.
Who should wear a mask? ▪ Patients with infectious TB or suspected infectious TB	Who should wear a respirator? ▪ Staff Note: Visitors to TB isolation rooms should be restricted. Unless persons have been fit tested, they may not be protected by wearing N-95 masks. Consult your facility's infection control plan for guidance.
A patient should wear a mask In a hospital setting when: ▪ Suspected of having infectious TB and not yet placed in respiratory isolation ▪ Leaving a respiratory isolation room for any reason Note: Infectious patients should NOT wear masks when in their TB isolation rooms. In a health clinic setting when: ▪ Not in a TB isolation room ▪ Returning to the clinic for evaluation	A staff person or visitor should wear a respirator In a hospital or clinic setting when: ▪ Entering a TB isolation room ▪ Performing cough-inducing or aerosol-generating procedures ▪ Unlikely to be protected by administrative or environmental controls
A patient should wear a mask In a transportation setting when: ▪ Traveling in a vehicle with other persons	A staff person or visitor should wear a respirator In some transportation settings when: ▪ Riding in a vehicle with a patient with infectious TB
In the patient's home: Note: Infectious patients do NOT need to wear a mask when they are in their homes.	A staff person should wear a respirator in a patient's home when: ▪ Visiting the infectious patient inside a home/residence Note: There should NOT be any visitors (excluding protected healthcare workers) in the home until the patient is released from TB isolation.

Definition of abbreviations: NIOSH = National Institute for Occupational Safety and Health; TB = tuberculosis.

* There are some devices, such as the 3M 1860, which are both N95 respirators and surgical masks.

Source: CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):38–40.

Employee Health

All employees, physicians, and volunteers who have potential for exposure to *Mycobacterium tuberculosis* should be screened for tuberculosis at hire, and at least annually thereafter by tuberculin skin test (TST) or interferon gamma release assay (IGRA), if indicated by the settings' TB infection control policies or TB risk classification, and complete a TB symptom review questionnaire.[23]

Two-Step Tuberculin Skin Testing

Two-step testing is used to improve the interpretation of tuberculin skin tests (TSTs), especially in persons who need to receive serial tests. Two-step testing should be used for the **initial** skin testing of adults who will be retested periodically, such as healthcare workers.[24]

In some persons who are infected with *Mycobacterium tuberculosis,* delayed-type hypersensitivity to tuberculin may wane over the years. When these persons are skin tested many years after their infection, they may have a negative reaction.

However, the skin test may have stimulated (boosted) their ability to react to tuberculin, causing a positive reaction to subsequent tests. This boosted reaction may be misinterpreted as a new infection. The booster phenomenon may occur at any age, but its frequency increases with age and is highest among older persons. Boosted reactions may occur in persons infected with nontuberculous mycobacteria or in persons who have had a prior Bacille Calmette-Guérin (BCG) vaccination.

A positive reaction to the second test should be interpreted as evidence for infection with *M. tuberculosis.* On the basis of this second test result, the person should be classified as previously infected and cared for accordingly. This would not be considered a skin test conversion.

If the first and second test results are negative, the person should be classified as uninfected. In these persons, a positive reaction to any subsequent test is likely to represent new infection with *M. tuberculosis* (a skin test conversion). Schedule apppointments for two-step testing as shown below.

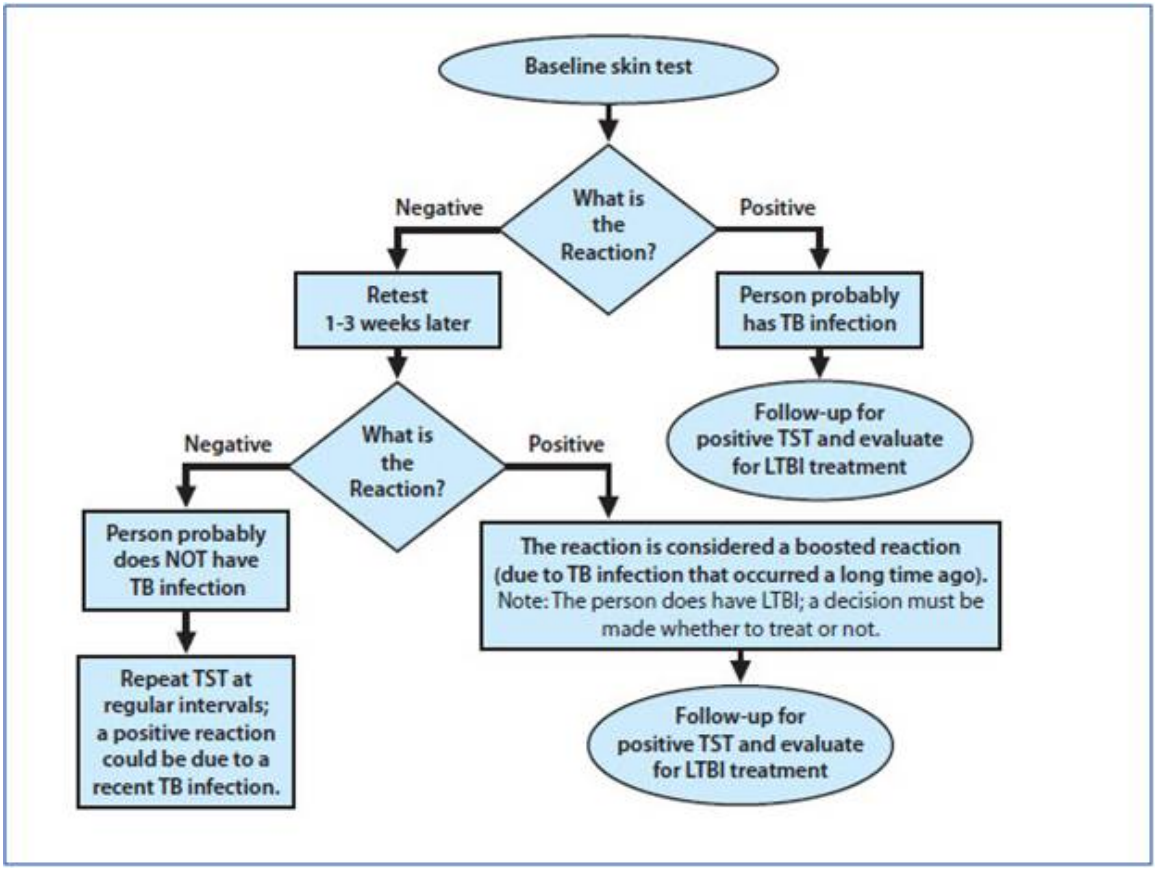
Refer to the topics on administration, measurement, and interpretation of the tuberculin skin test in the section on Diagnosis of Latent Tuberculosis Infection **7.7**.

Table 3: FOUR APPOINTMENT SCHEDULE FOR TWO-STEP TESTING

Appointments	Tasks
First appointment	Apply the first tuberculin skin test (TST).
Second appointment 48 to 72 hours after applying the first TST	Measure the reaction. ▪ If the reaction is negative, schedule a third appointment. ▪ If the reaction is positive, do not repeat the TST. Obtain a chest radiograph.
Third appointment 1 to 3 weeks after measurement of the first TST	Re-apply the TST. ▪ Use the same dose and strength of tuberculin. Inject the tuberculin on the other forearm, or at least 5 cm from the original test site. ▪ If the reaction is negative and the patient returns over a week after the first TST was applied, apply the second TST.
Fourth appointment 48 to 72 hours after applying the second TST	Measure the reaction. ▪ If the reaction is negative, classify the individual as uninfected. ▪ If the reaction is positive, obtain a chest radiograph.

* All TST results should be read and recorded by a trained TST reader other than the person on whom the TST was placed.[25]

Figure 1: TWO STEP TESTING AND FOLLOW-UP



For more information on two-step testing, refer to the CDC's "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Facilities, 2005" (*MMWR* 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf.

Screening for persons with previously positive TST, IGRA or completion of treatment for LTBI or active TB

Employees, physicians, and volunteers who have written documentation of a previous positive TST result may be required to have a baseline chest x-ray at hire or provide written documentation of a normal chest x-ray taken no more than 12 months prior to hire. The chest x-ray will be repeated only if the employee develops signs or symptoms of TB or when the attending physician decides a repeat chest x-ray is needed. Screening is conducted, at least annually, via a TB symptom review questionnaire instead of TST or IGRA for previously positive employees. If the symptom screen reveals signs or symptoms of TB, the employee will be excluded from the workplace. A new chest x-ray and physical assessment is then required.[26]

A sample TB symptom review questionnaire can be found in Francis J Curry International Tuberculosis Center, 2007:Tuberculosis Infection Control: A Practical Manual for Preventing TB [1-171]. Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12CD

Isolation

To reduce disease transmission, a patient with tuberculosis (TB) disease may need to be isolated or have activities restricted.

Isolation: Isolation is used when people are ill. Isolation of people who have a specific illness separates them from healthy people and restricts their movement to stop the spread of that illness. Isolation allows for the focused delivery of specialized health care to people who are ill, and it protects healthy people from getting sick. People in isolation may be cared for in their homes, in hospitals, or at designated healthcare facilities. Isolation is a standard procedure used in hospitals today for patients with TB and certain other infectious diseases. In most cases, isolation is voluntary; however, many levels of government (federal, state, and local) have the basic legal authority to compel isolation of sick people to protect the public.[27]

Restricted Activities: Until determined to be noninfectious, the patient is not permitted to return to work, school, or any social setting where the patient could expose individuals to airborne bacteria.

Quarantine: Although TB control programs have used the word “quarantine” interchangeably with “isolation” and “restricted activities,” the word “quarantine” properly used is not a term applicable to TB control. Quarantine applies to people who have been exposed and may be infected but are not yet ill. Separating exposed people and restricting their movements is intended to stop the spread of illness. Quarantine is not an appropriate TB control measure for asymptomatic, exposed individuals. [28]

For information on diagnosis and laboratory tests, refer to the sections on diagnosis of tuberculosis disease and latent tuberculosis infection. For information on guidelines for infection control in the patient’s residence, group settings, and during transportation of a patient, see the subtopics that follow.

Estimating Infectiousness

In general, patients who have suspected or confirmed TB disease and who are not on antituberculosis treatment should be considered infectious if characteristics include the following:

- Presence of cough
- Cavitation on chest radiograph
- Positive acid-fast bacilli (AFB) sputum smear result
- Respiratory tract disease with involvement of the lung or airways, including larynx
- Failure to cover the mouth and nose when coughing
- Undergoing cough-inducing or aerosol-generating procedures (e.g., sputum induction, bronchoscopy, airway suction) [29]

If a patient with one or more of these characteristics is on standard multidrug therapy with documented clinical improvement, usually in connection with smear conversion over several weeks, the risk of infectiousness is reduced.[30]

Determining Noninfectiousness

Use the following criteria as general guidelines to determine when during therapy a patient with pulmonary TB disease has become noninfectious. Decisions about infectivity of a person on treatment for TB should depend on the extent of illness and the specific nature and circumstances of the contact between the patient and exposed persons. These guidelines can and should be modified on a case-by-case basis by a qualified public health officer or health officer.

- Patient has negligible likelihood of multidrug-resistant TB (no known exposure to multidrug-resistant tuberculosis and no history of prior episodes of TB with poor compliance during treatment).
- Patient has received standard multidrug antituberculosis therapy for at least two weeks.
- Patient has demonstrated complete adherence to treatment (e.g., is receiving directly observed therapy).
- Patient has demonstrated evidence of clinical improvement (e.g., reduction in the frequency of cough or reduction of the grade of the AFB sputum smear result).
- ll close contacts of the patient have been identified, evaluated, advised, and, if indicated, started on treatment for latent TB infection. This criterion is critical, especially for children younger than 5 years of age and persons of any age with immunocompromising health conditions such as human immunodeficiency virus (HIV) infection.

Table 4: CRITERIA FOR PATIENTS TO BE CONSIDERED NONINFECTIOUS

Patients can be considered noninfectious when they meet the following three criteria:
1. They have three consecutive AFB-negative sputum smear results from specimens collected eight to 24 hours apart, with at least one being an early morning specimen. **2.** They have demonstrated clinical improvement (for example, they are coughing less and they no longer have fever); **and** 3. They have received at least two weeks of standard multidrug antituberculosis therapy

While in hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they meet the criteria in Table 4 above.

Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected more than eight hours apart before being considered noninfectious.[31]

Airborne Infection Isolation in a Healthcare Facility

In airborne infection isolation (AII), the patient is placed in an AII room, usually within a hospital or healthcare facility. The main characteristics of an AII room (for new or renovated buildings) are that it has negative air pressure relative to the hall and **12 or more air exchanges per hour**, of which at least two exchanges are outside air. For existing structures, six or more air exchanges per hour are acceptable.

See Table 5 : **Air changes per hour (ACH) and time required for removal efficiencies of 99% and 99.9% of airborne contaminants*** [32] for information on estimating the time necessary to clear the air of airborne *Mycobacterium complex* after the source patient leaves the area or the aerosol-producing procedures are complete.

Table 5 : **Air changes per hour (ACH) and time required for removal efficiencies of 99% and 99.9% of airborne contaminants*** [33]

Air changes per hour (ACH) and time in minutes required for removal efficiencies of 99% and 99.9% of airborne contaminants* [34]		
ACH	99%	99.9%
2	138	207
4	69	104
6	46	69
12	23	35
15	18	28
20	14	21
50	6	8
400	<1	1

*Time in minutes to reduce airborne concentration by 99% or 99.9%.

The decisions to initiate and discontinue isolation should be made in consultation with the Infection Preventionist. Isolation decisions should be made on a case-by-case basis.

When to Initiate Airborne Infection Isolation

Suspected cases of laryngeal or pulmonary TB should be isolated immediately, before AFB sputum smear results are available.

Initiate TB AII precautions for any patient who meets the criteria in Table 6.

Table 6: INITIATION OF AIRBORNE INFECTION ISOLATION[35]

Criteria for Initiation of Airborne Infection Isolation		
The patient has signs or symptoms of pulmonary, laryngeal, or multidrug-resistant tuberculosis (MDR-TB) disease	OR	▪ The patient has documented infectious pulmonary, laryngeal tuberculosis (TB) disease or MDR-TB disease AND ▪ The patient has not completed treatment

Source: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):16, 44.

Patients with suspected or confirmed MDR-TB should remain in an AII room throughout their hospitalization or until culture conversion is documented, regardless of sputum smear results.

When to Discontinue Airborne Infection Isolation

Prior to discontinuing isolation, call the Infection Preventionist. High-risk patients should be carefully evaluated before discontinuing isolation. Hospitalized patients with suspected or confirmed MDR-TB should remain in an AII room throughout their hospitalization.

Suspected Tuberculosis Disease

For patients placed in AII due to suspected infectious TB disease of the lungs, airway, or larynx, AII can be discontinued when the criteria in Table 7 are met.

Table 7: DISCONTINUATION OF AIRBORNE INFECTION ISOLATION OF SUSPECTED CASES OF TUBERCULOSIS[36]

Criteria for Discontinuing Airborne Infection Isolation: Suspected Case of Tuberculosis of the Lungs, Airway, or Larynx		
Infectious tuberculosis (TB) disease is considered unlikely	AND	Either ▪ Another diagnosis is made that explains the clinical syndrome OR ▪ The patient has 3 negative acid-fast bacilli (AFB) sputum smear results* has been on treatment delivered as directly observed therapy for al least 2 weeks, and has demonstrated clinical improvement
* Each of the 3 sputum specimens should be collected 8 to 24 hours apart, and at least 1 should be an early morning specimen (because respiratory secretions pool overnight). Generally, this will allow patients with negative AFB sputum smear results to be released from AII in 2 days.[37]		
While in the hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they (1) are receiving standard multidrug antituberculosis therapy; (2) have demonstrated clinical improvement; and (3) have had 3 consecutive AFB-negative smear results of sputum specimens collected 8 to 24 hours apart, with at least 1 being an early morning specimen.[38]		
Because patients with TB disease who have negative AFB sputum smear results can still be infectious, patients with suspected disease who meet the above criteria for release from AII should not be released to an area where other patients with immunocompromising conditions or children <5 years are housed.[39]		

Sources: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):16, 43; ATS, CDC. 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):9

Confirmed Tuberculosis Disease

A patient with drug-susceptible TB of the lung, airway, or larynx who is on standard multidrug antituberculosis treatment and who has had a significant clinical and bacteriologic response to therapy (e.g., reduction in cough, resolution of fever, and progressively decreasing quantities of AFB on smear results) is probably no longer infectious. However, because culture and drug susceptibility results are not usually known when the decision to discontinue AII is made, all patients with confirmed TB disease should remain in AII while hospitalized until all the criteria in Table 8 are met.[40]

Table 8: DISCONTINUATION OF AIRBORNE INFECTION ISOLATION OF CONFIRMED CASES OF TUBERCULOSIS[41]

Criteria for Discontinuing Airborne Infection Isolation: Hospitalized Patients with Confirmed, Drug-Susceptible Tuberculosis of the Lungs, Airway, or Larynx
▪ The patient has had 3 consecutive negative acid-fast bacilli (AFB) sputum smear results collected 8 to 24 hours apart, with at least 1 being an early morning specimen AND ▪ The patient has received at least 2 weeks of standard multidrug antituberculosis treatment by directly observed therapy (DOT) AND ▪ The patient has demonstrated clinical improvement

Source: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):43.

Hospital Discharge

The decisions to discharge an AFB sputum smear-positive patient or an MDR-TB patient should be made in consultation with Infection Preventionist, the Alaska Tuberculosis Program, local Public Health Nurse (PHN), and the primary care provider.

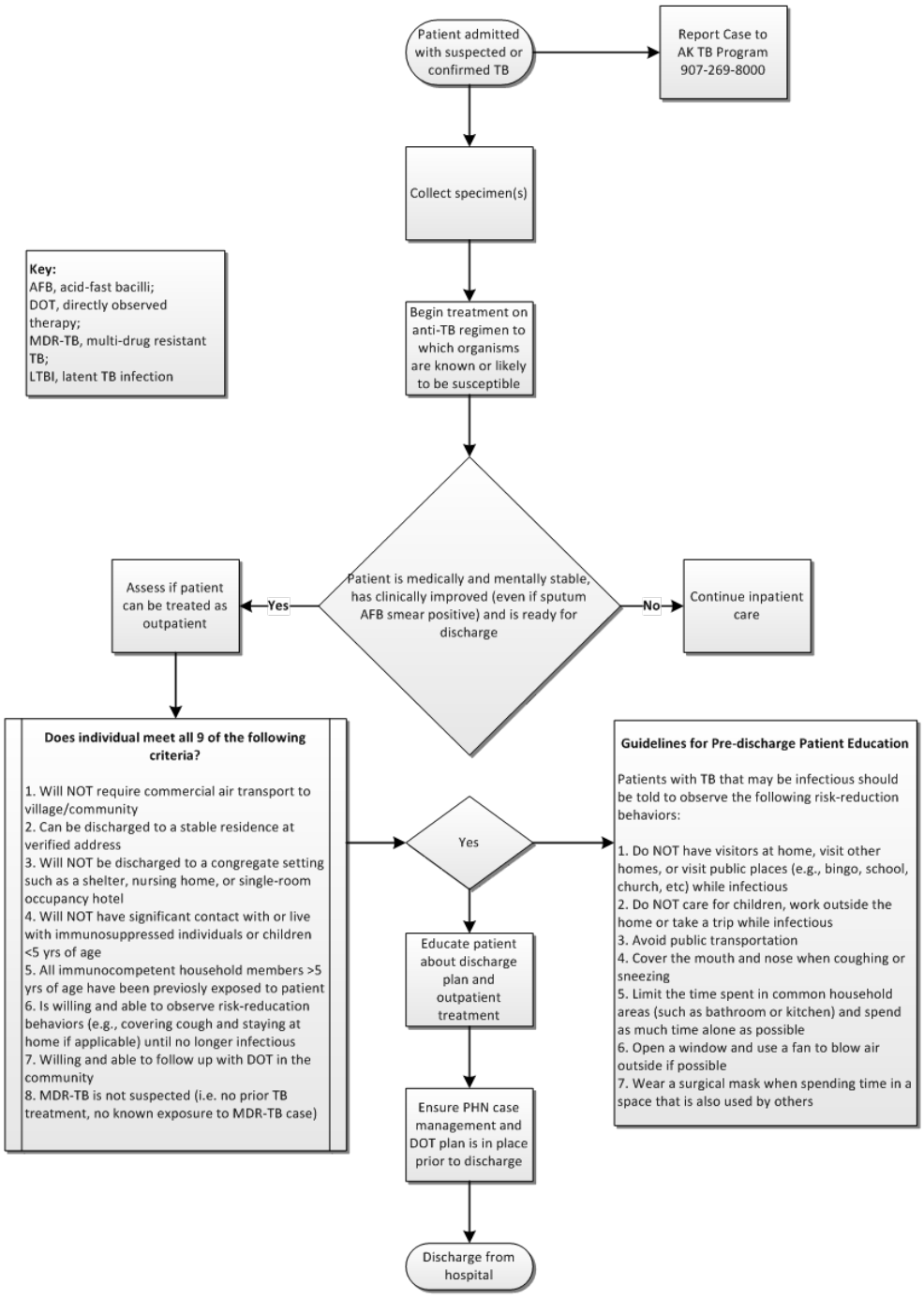
Use the *Tuberculosis Discharge Planning Checklist* to guide discharge planning. It is available in the Forms section of the manual **18.1**.

Call the Alaska TB Program for consultation regarding discharge planning and coordination with the local PHN – 907-269-8000.

Drug-Susceptible Tuberculosis Disease

If a hospitalized patient who has suspected or confirmed drug-susceptible TB disease is deemed medically stable (including patients with positive AFB sputum smear results indicating pulmonary TB disease), the patient can be discharged from the hospital before converting AFB sputum smear results to negative if all the criteria in Figure 2 are met.[42]

Figure 2. Criteria for Discharging Patients with Suspected or Confirmed Tuberculosis from the Hospital



Adapted from: New York Department of health and Mental Hygiene, Bureau of Tuberculosis Control, Clinical Policies and Protocols, 4th Edition. March 2008.

Table 9: HOSPITAL DISCHARGE OF DRUG-SUSCEPTIBLE CASES OF TUBERCULOSIS[43]

Criteria for Hospital Discharge to Home: Patients with Suspected or Confirmed Drug-Susceptible Tuberculosis
▪ A specific plan exists for follow-up care with the local PHN and Alaska TB Program AND ▪ The patient has been started on a standard multidrug antituberculosis treatment regimen and directly observed therapy (DOT) has been arranged AND ▪ No children aged <5 years or persons with immunocompromising conditions are present in the household AND ▪ All immunocompetent household members have been previously exposed to the patient AND ▪ The patient is willing to not travel outside the home except for healthcare-associated visits until the patient has negative acid-fast bacilli (AFB) sputum smear results

Source: CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):43–44.

Multidrug-Resistant Tuberculosis Disease

Patients with suspected or confirmed MDR-TB disease should remain in the hospital in AII until they meet all three of the criteria in Table 10.

Table 10: HOSPITAL DISCHARGE OF MULTIDRUG-RESISTANT CASES OF TUBERCULOSIS

Criteria for Hospital Discharge to Home: Patients with Suspected or Confirmed Multidrug-Resistant TB
▪ The patient has had 3 consecutive negative acid-fast bacilli (AFB) sputum smear results collected 8 to 24 hours apart, with at least 1 being an early morning specimen AND ▪ An appropriate treatment regimen has been devised and at least 2 weeks of multidrug therapy has been given by directly observed therapy (DOT) AND ▪ The patient has demonstrated clinical improvement ▪ Suitable arrangements have been made so that the regimen can be continued and properly monitored on an outpatient basis, specifically by (DOT)

Release Settings

Patients with suspected or confirmed infectious TB disease should not be released to healthcare settings or homes where the patient can expose others who are at high risk for progressing to TB disease if infected, such as HIV-infected persons or young children.[44] Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected more than eight hours apart before being considered noninfectious.[45]

Patients who have positive AFB sputum smear results should **not** be directly discharged from the hospital to **any** of the following living environments:

- Congregate living site (e.g., shelter, nursing home, jail, prison, group home, another hospital)
- Living situation where infants and young children also reside
- Living situation where immunosuppressed persons (e.g., HIV-infected persons or those taking cancer chemotherapy) also reside
- Living situation where home health aides or other social service providers will be present in the home for several hours a day to care for the person or family member

Residential Settings

Patients suspected of having infectious tuberculosis (TB) either are diagnosed during an outpatient workup, or if admitted to a hospital, are often sent home after starting treatment. Patients are sent home, even though they may still be infectious, because they are most likely to transmit TB to household members **before** TB has been diagnosed and treatment has started. However, TB patients and members of their household can take steps to prevent the spread of TB in their home until the patient becomes noninfectious.[46,47]

Administrative Controls in the Patient's Home

Have a policy and procedure for managing infectious patients at home. To standardize care, the following information should be included:

1. **Definition of key terms:** Infectious case and noninfectious case
2. **Treatment of cases at home whenever possible:** Treat patients at home if their condition does not otherwise require hospitalization.
3. **Window period treatment policy:** Ensure that candidates for window period treatment in the home have completed their evaluation and are on medication before they are discharged home (or as soon as possible if they were not hospitalized).
4. **Education:** Educate infectious patients, family, care providers, and close contacts regarding the purpose of isolation, their responsibility to adhere to the isolation requirements, and the consequences of not voluntarily complying with isolation.
5. **Home isolation agreements:** Have infectious cases in isolation sign a home isolation agreement. This document should include any legal consequences should they fail to voluntarily comply.

The *Tuberculosis Treatment Contract* may be used to document plans for home isolation. It can be found in the Forms section of the manual **18.1**.

Environmental Controls in the Patient's Home

Generally, there are no special engineering recommendations. However, patients and their families can be advised to do the following:

- Have tissues available for patients to cover their mouths and noses when coughing or sneezing.
- Keep windows and doors open (weather permitting) to increase the ventilation and dilution of infectious droplet nuclei in the house.
- If a sputum sample needs to be collected at home, do so in a well-ventilated area away from other residents (e.g., bathroom with an exhaust fan). If possible, collect the sputum in an outdoor area away from open windows or doors.

Respiratory Protection in the Patient's Home

Patient: Mask

- Patients do not need to wear masks at home.
- Give patients regular surgical-type masks and advise them to wear them at medical appointments until they are no longer infectious.
- Do not give patients respirators (N-95 or higher).

For more information on the criteria for noninfectiousness, see the "Determining Noninfectiousness" topic in this section **17.16**.

Healthcare Worker: Respirator

- Healthcare workers should wear respirators when entering the home or a closed area to visit with infectious patients.
- The respirators should be National Institute for Occupational Safety and Health (NIOSH)-approved (N-95 or higher).
- Healthcare workers should be provided with respirators after appropriate education and fit testing.

Other Residential Settings

Motels

Homeless persons with infectious TB may be housed in a motel that has outside access to rooms (not via hallways).

The motel manager must be advised of the following:

1. The patient is in respiratory isolation.
2. The manager should report to local public health agency staff if the manager becomes aware that the patient does not stay in the room or has guests.
3. The manager should advise motel staff that they are not to enter the room while the patient resides at the motel. (Arrangements should be made that once a week, the patient sets out linens that need to be replaced. The staff can knock on the door and leave the linens for the patient to make his or her own bed.)
4. Upon release from isolation, the room should be aired out for one day before staff enter to clean. Afterwards, routine cleaning done between guests is sufficient, and there are no additional special cleaning requirements.
5. Local public health agency staff will be delivering medication to the patient (specify the frequency).
6. Arrangements have been made for food delivery to the patient.

Healthcare Facilities or Residential Settings

1. Patients with infectious TB should be in appropriate respiratory isolation (airborne infection isolation rooms) when housed in healthcare facilities or residential settings.
2. If a facility does not have the capability to provide appropriate respiratory isolation, the patient should be transferred to a facility that can accommodate respiratory isolation until the patient is noninfectious. Once noninfectious, the person may return to the original facility.

Return to Work, School, or Other Social Settings

The decision of when to allow a patient to return to work, school, or other social settings should be made in consultation with the Alaska TB Program and/or the local PHN.

The decision to permit a patient to return to work, school, or other social settings is based on the following:

- The characteristics of the patient with TB disease (e.g., whether the patient is likely to adhere to the regimen and follow treatment instructions)
- The characteristics of the TB disease itself (e.g., multidrug-resistant versus drug-susceptible TB, AFB sputum smear-positive versus smear-negative, cavitary versus noncavitary)
- The duration of current treatment (e.g., the patient has received standard multidrug antituberculosis therapy for two-to-three weeks or, if the patient AFB sputum smear that are negative or rarely positive, the threshold for treatment is four-to-seven days)[48]
- The environment(s) to which the patient will be returning

Prior to notifying a patient that he or she is able to return to work or school, call the Alaska TB Program at 907-269-8000 for consultation.

Drug-Susceptible Tuberculosis Disease

Patients with drug-susceptible TB are no longer considered infectious if they meet all the criteria in Table 11.

Table 11: RETURN TO WORK, SCHOOL, AND OTHER SETTINGS OF DRUG-SUSCEPTIBLE CASES OF TUBERCULOSIS[49]

Criteria for Return to Work, School, or Other Social Settings: Patients with Suspected or Confirmed Drug-Susceptible Tuberculosis
▪ The patient is on adequate therapy for at least 2 weeks AND ▪ The patient has had a significant clinical response to therapy AND ▪ The patient has had 3 consecutive negative acid-fast bacilli (AFB) sputum smear results collected 8 to 24 hours apart, with at least 1 being an early morning specimen

Source: CDC. Module 5: Infectiousness and Infection control. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2016. Available at: https://www.cdc.gov/tb/education/ssmodules/pdfs/tb_selfstudymodules_2015_module05.pdf . Accessed January 18, 2017.

Multidrug-Resistant Tuberculosis (MDR-TB) Disease

Regardless of their occupation, patients known or likely to have pulmonary MDR-TB may be considered for return to work or school only if they meet all four of the criteria in Table 12.

Table 12: RETURN TO WORK, SCHOOL, AND OTHER SETTINGS OF MULTIDRUG-RESISTANT CASES OF TUBERCULOSIS

Criteria for Return to Work, School, or Other Social Settings: Patients with Suspected or Confirmed Multidrug-Resistant TB
▪ The resolution of fever and the resolution, or near resolution, of cough has occurred AND ▪ The patient is on current treatment with an antituberculosis regimen to which the strain is known or likely to be susceptible for at least 2 weeks AND ▪ The patient has had 3 consecutive negative acid-fast bacilli (AFB) sputum smear results collected 8 to 24 hours apart, with at least 1 being an early morning specimen AND ▪ The patient has had a negative culture for *Mycobacterium tuberculosis*
*In addition, directly observed therapy (DOT) should be strongly encouraged for patients with MDR-TB.

Tuberculosis Infection Control in Patient Care Facilities

Patients with suspected tuberculosis (TB) may present for care in many different settings. The Centers for Disease Control and Prevention (CDC) has written a comprehensive set of guidelines for TB infection control in acute care hospitals and other medical settings.[50] In addition to the CDC guidelines, various professional organizations or state regulations may have guidelines for managing TB patients.

The main focus in establishing a TB infection control program at a patient care facility is to:

1. assign responsibility for managing the program to a designated staff position;
2. perform and establish a TB risk assessment for the facility; and
3. develop the TB infection control plan based on the level of TB risk identified in the assessment.

The main purpose for having an effective TB infection control plan in a facility is to assure that the activities necessary for TB control are addressed and that policies and procedures are developed to protect the healthcare workers, other patients, and visitors in the facility.

Table 13: **Guidelines for Tuberculosis Infection Control** lists references that provide the information needed to conduct a TB risk assessment and write a TB infection control plan to establish policies and procedures for TB control activities inpatient care facilities.

Call the Alaska TB Program at 907-269-8000 if you have any questions when consulting with institutions on infection control measures.

Table 13: GUIDELINES FOR TUBERCULOSIS INFECTION CONTROL

Guidelines for Tuberculosis Infection Control

The following settings are addressed in the "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Facilities, 2005" (MMWR 2005;54[No. RR-17]) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf
Some settings have additional guidelines as noted below.

Inpatient Settings

- Emergency departments and urgent care settings
- Intensive care units
- Surgical suites
- Laboratories
- Bronchoscopy suites
- Sputum induction and inhalation therapy rooms
- Autopsy suites and embalming rooms

Outpatient Settings

- Tuberculosis (TB) treatment facilities
- Medical settings in correctional facilities: Prevention and Control of Tuberculosis in Correctional Facilities. (ACET) (*MMWR* 1996;45[No. RR-8]) at http://www.cdc.gov/MMWR/PDF/rr/rr4508.pdf
- Medical offices and ambulatory care settings
- Dialysis units

Nontraditional Facility-Based Settings

- Homeless shelter clinics: Prevention and Control of Tuberculosis Among Homeless Persons (ACET) (*MMWR* 1992;41[No. RR-5]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/00019922.htm
- Emergency medical services
- Home-based healthcare and outreach settings
- Long-term care facilities (e.g., hospices, skilled nursing facilities): Prevention and Control of Tuberculosis in Facilities Providing Long-Term Care to the Elderly (*MMWR* 1990;39[No. RR-10]) at http://www.cdc.gov/mmwr/preview/mmwrhtml/00001711.htm

Other References

- Curry International Tuberculosis Center, 2007:Tuberculosis Infection Control: A Practical manual for Preventing TB [1-171]. Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12CD

Transportation Vehicles

To prevent the transmission of *M. tuberculosis* while transporting patients, follow the respiratory precautions identified below.

Patient Self-Transport

1. The car windows should be opened, and any recirculating air controls should be turned off.
2. If possible, only household members should accompany the patient. Any members of the patient's household who accompany the patient do not need to wear surgical masks.
3. If the only source for transport is a friend or relative who is not a member of the patient's household:
   a. The patient should sit in the back seat and wear a surgical mask.
   b. The car windows should be opened, and any recirculating air controls should be turned off. .
   c. The person accompanying the patient should be given a mask to wear during transport (due to the confined space and lack of ongoing exposure).
4. The patient should wear a surgical mask after leaving the vehicle.[51]

Transport by Healthcare Workers

1. Healthcare workers should wear respiratory protection (N-95) while in the vehicle.
2. The patient should wear a surgical mask and sit in the back seat.
3. The car windows should be opened, and any recirculating air controls should be turned off. [52]

Transport by Emergency Medical Services

Emergency medical services staff have specialized vehicles that may have the ability to separate the driver's compartment from the transport compartment and rear exhaust fans. Recommendations for these vehicles and staff are addressed in the Centers for Disease Control and Prevention (CDC) "Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Facilities, 2005" (*MMWR* 2005;54[No. RR-17]:25–26, 88, 127) at http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf .

Resources and References

Resources

- CDC. “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
- CDC. “Guidelines for Environmental Infection Control in Health-care Facilities“ (*MMWR* 2003;52[No. RR-10]) at http://www.cdc.gov/mmwr/PDF/rr/rr5210.pdf
- CDC. *Interactive Core Curriculum on Tuberculosis* 2011 at http://www.cdc.gov/tb/education/ce/interactive-corecurr.htm
- CDC. “Respiratory Protection in Health-Care Settings” (*TB Elimination Fact Sheet* April 2010) at http://www.cdc.gov/tb/publications/factsheets/prevention/rphcs.pdf
- CDC. Module 4: “Treatment of TB Infection and Disease” (*Self-Study Modules on Tuberculosis 2008*) at http://www.cdc.gov/tb/education/ssmodules/pdfs/Module4.pdf
- CDC. Module 5: “Infectiousness and Infection Control” (*Self-Study Modules on Tuberculosis 2008*) at http://www.cdc.gov/tb/education/ssmodules/pdfs/Module5.pdf
- NIOSH. “Respiratory Protection” [Web page] at http://www.cdc.gov/niosh/topics/respirators/
- OSHA. “Tuberculosis: OSHA Standards” [Web page] at http://www.osha.gov/SLTC/tuberculosis/index.html
- Curry International Tuberculosis Center, 2007:Tuberculosis Infection Control: A Practical Manual for Preventing TB [1-171]. Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12CD
- Curry International Tuberculosis Center, 2009: Practical Solutions for TB Infection Control: Infectiousness and Isolation. Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=ONL-13

References

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[6] CDC. Prevention and control of tuberculosis in correctional facilities. (ACET) *MMWR* 1996;45(No. RR-8).

[7] CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):7.
[8] CDC. Essential components of a tuberculosis prevention and control program: screening for tuberculosis and tuberculosis infection in high-risk populations. *MMWR* 1995;44(No.RR-11):3.
[9] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):8.
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[11] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):8.
[12] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):9.
[13] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):8.
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[16] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):75.
[17] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):77.
[18] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):78.
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[27] CDC. Public Health Measures in Response to SARS: Isolation, Quarantine, and Community Control. *Severe Acute Respiratory Syndrome Fact Sheet.* September 11, 2003:1.
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34 CDC. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care facilities, 2005. MMWR 2005;54(No. RR-17):20
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[36] CDC. Guidelines for preventing the transmission *of Mycobacterium tuberculosis* in health-care facilities, 2005. *MMWR* 2005;54(No. RR-17):16, 43.
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Forms:

Alaska TB Program: Timeline for Case Management of Tuberculosis Treatment

Anchorage State Public Health Laboratory Request Form – Fillable form: http://dhss.alaska.gov/dph/Labs/Documents/publications/AncSupplyReq.pdf

Consent for Release of Medical Information

Contact Investigation Form (3 pages)

Contact Investigation Form – Instructions

DOT Calendar

DOT Job Description (2 pages)

DOT Memorandum of Agreement

DOT Monthly Invoice for Payment

DOT Plan

End of Treatment Letter and Summary (2 pages)

Infectious Disease Report Form – Fillable form: http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/frmInfect.pdf

Interjurisdictional TB Notification – Fillable form: http://www.tbcontrollers.org/docs/resources/IJN_Form_May2015.pdf

Interjurisdictional TB Notification Follow-Up – Fillable form: http://www.tbcontrollers.org/docs/resources/IJN_FollowUpForm_November2014.pdf

Liver Function Test Flowsheet

LTBI Treatment Completion Form and Instructions (2 pages)

PPD Order Form

Referral and Authorization for TB Screening and Follow-Up Services (2 pages)

Sputum Collection Guidelines

TB Case Management Form

TB Case Management Information Request

TB Discharge Planning Checklist

TB Medication Drug Count Worksheet

TB/LTBI Medication Request

TB/LTBI Medication Request - Guidelines

TB/LTBI Medication Return Form and Guidelines (3 pages)

TB/LTBI Stock TB Medication Request and Guidelines (2 pages)

Tuberculosis Screening Questionnaire/Chest X-ray Interpretation Request (2 pages)

Tuberculosis Screening Questionnaire Guidelines

Tuberculosis Treatment Contract (2 pages)

Statutes and Regulations

CONTENTS

Introduction

Purpose

Use this section to access Alaska statutes and regulations that pertain to the prevention and control of tuberculosis in Alaska.

Conditions Reportable to Public Health Manual

Basic information and links to the both the Alaska Statutes and the Alaska Administrative Code, or regulations, are available in the ***Conditions Reportable to Public Health Manual*** and will not be included here. Infection control, employee health, and school screening regulations are included in this section.

Suspected or confirmed cases of tuberculosis are reportable by both health care providers and laboratories in Alaska. See the Surveillance section of this manual for more information **2.9**.

Alaska Statutes and Regulations pertaining to the control of tuberculosis in Alaska are available in the *Conditions Reportable to Public Health Manual* at http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/ConditionsReportable.pdf

Call the Alaska TB Program for consultation regarding State Statutes and Regulations – 907-269-8000.

Regulations

Infection Control

7 AAC 12.566. Infection control

(a) A home health agency shall develop and implement written policies and procedures applicable to all agency staff that

(1) minimize the risk of transmitting infection in all patient care or services; and

(2) provide for the safe handling and disposal of biohazardous and infectious materials.

(b) At least every two years, a home health agency shall verify that its employees, contractors, and volunteers who provide patient care receive training on universal precautions and the prevention, transmission, and treatment of

(1) human immunodeficiency virus (HIV);

(2) acquired immunodeficiency virus (AIDS);

(3) hepatitis; and

(4) tuberculosis.

History: Eff. 9/6/96, Register 139

Authority: AS 18.05.040

Employee Health Programs

7 AAC 12.571. Employee health program

(a) Except as provided in (b) - (e) of this section, a home health agency shall have an employee health program that requires each employee to be tested for pulmonary tuberculosis within the first two weeks of initial employment and annually thereafter. The home health agency shall require contractors performing patient care or services for the agency to have similar standards in place.

(b) An employee who has never had a positive tuberculin skin test result must have a tuberculin Mantoux skin test. A further annual tuberculin testing is not necessary if the

(1) test is negative;

(2) employee is never required to be in a room where a patient or resident might enter; and

(3) employee does not handle clinical specimens from a patient or other material from a patient's room.

(c) An employee who has a positive tuberculin skin test result, or previously had a positive tuberculin skin test result, must have a health evaluation to determine if tuberculosis disease is present. If the presence of tuberculin disease is confirmed, the employee shall be removed from direct contact with patients until the employee has received written verification from a physician that the employee is determined to be noncontagious.

(d) If the employee has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the employee need not have further annual tuberculosis evaluation.

(e) A home health agency that provides care to pregnant women shall document that each employee who provides direct patient care has been immunized against rubella by having on file

(1) a valid immunization certificate signed by a physician or registered nurse listing the date of rubella vaccination;

(2) a copy of a record from a clinic or health center showing the date of rubella vaccination; or

(3) the result of a serologic test showing the employee is immune.

History: Eff. 9/6/96, Register 139

Authority: AS 18.05.040

7 AAC 12.650. Employee health program

Note: the term “facility” is defined in 7 AAC 12.990 to mean a general acute care hospital, specialized hospital, nursing home, intermediate care facility for the mentally retarded, ambulatory surgical center, birth center, mental health center, home health agency, rural primary care hospital, and critical access hospital.

(a) Each facility must have an employee health program that

(1) requires each employee to be evaluated within the first two weeks of employment and, except as provided otherwise in this paragraph, annually after that, to detect active cases of pulmonary tuberculosis, as follows:

(A) an employee who has never had a positive tuberculin skin test result shall obtain a tuberculin Mantoux skin test; if the tuberculin skin test result is negative, the employee does not need to have further annual tuberculosis evaluation under this paragraph if the employee's duties never require him or her to be in a room where patients or residents might enter, and if the employee does not handle clinical specimens or other material from patients or from their rooms; an example of such an employee is an administrative person or research worker whose

place of work is remote from patient or residential care areas and who does not come in contact with clinical specimens;

(B) an employee who has previously had a positive tuberculin skin test result, or an employee whose tuberculin skin test obtained under (A) of this paragraph has a positive result,

(i) shall have a health evaluation by a health care provider to identify symptoms suggesting that tuberculosis disease is present; the health evaluation must also include evaluation for the presence of any of the following risk factors: evidence of inadequately treated past tuberculosis disease, history of close exposure to a case of communicable pulmonary tuberculosis within the previous two years, history of a negative tuberculin test within the previous two years, diabetes mellitus (severe or poorly controlled), diseases associated with severe immunologic deficiencies, immunosuppressive therapy, silicosis, gastrectomy, excessive alcohol intake, or human immunodeficiency virus infection; if symptoms suggesting tuberculosis disease are present, or if any of the risk factors is present, a chest x-ray shall be obtained as part of the health evaluation and the health care provider shall report the case to the section of epidemiology, division of public health; and

(ii) if the employee has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the employee need not have further annual tuberculosis evaluation under this paragraph; and

(2) requires evidence of immunization against rubella by

(A) a valid immunization certificate signed by a physician listing the date of rubella vaccination;

(B) a copy of a record from a clinic or health center showing the date of vaccination; or

(C) the result of a serologic test approved by the department showing the employee is immune.

(b) The requirement of (a)(2) of this section does not apply to home health agencies, nursing homes, or ambulatory surgical facilities, and, for employees of other facilities, may be waived if a physician signs a certificate that there are medical reasons which dictate that an employee should not be vaccinated against rubella.

History: Eff. 11/19/83, Register 88; am 7/17/87, Register 103

Authority: AS 18.05.040

AS 18.20.010

AS 18.20.060

School Screening

7 AAC 27.213 Tuberculosis screening of school children

(a) Each public school district and nonpublic school offering pre-elementary education through the 12th grade, or a combination of these grades, shall assess the tuberculosis status of each child not later than 90 days after school enrollment. The department will inform each public school district and each nonpublic school about the appropriate tuberculosis screening strategy that the district or school shall employ. The strategy may consist of annual health surveys upon registration, PPD skin tests, alternative laboratory-approved methods for assessing tuberculosis status, or a combination of two or more of those approaches. The department will use one or more of the following criteria to determine the required screening strategy for a public school district or nonpublic school:

(1) evidence that prior PPD skin testing of school children in a community served by the district or school demonstrates tuberculosis transmission;

(2) evidence that tuberculosis disease is occurring in a community served by the district or school;

(3) evidence that a community served by the district or school has a history of high rates of tuberculosis when compared to rates of tuberculosis for the United States or this state;

(4) evidence that children from populations having a high risk of tuberculosis are enrolled in the district or school; in this paragraph, "populations having a high risk" includes groups that historically have been medically underserved, homeless persons, foreign-born persons from countries with high rates of tuberculosis, and persons with immune deficiency conditions.

(b) If the results of a health survey indicate an elevated risk for tuberculosis, or if a PPD skin test or other laboratory screening test is positive for tuberculosis, including a test result provided under (e) of this section, the public school district or nonpublic school shall refer the child to a health care provider and notify the department at the department's office in Anchorage.

(c) The public school district or nonpublic school shall record the result of a health survey, PPD skin test, or other laboratory test administered under this section in the permanent health record of the child.

(d) The public school district or nonpublic school shall suspend a child under AS 14.30.045

(4) if

(1) the district or school has not screened the child for tuberculosis; or

(2) the child or a person acting on behalf of the child fails to provide the district or school, within 30 days after referral under

(b) of this section, a written and signed statement of a health care provider stating that the child is not infectious from tuberculosis to others.

(e) Notwithstanding (a) - (d) of this section, a PPD skin test or alternative laboratory-approved method for assessing tuberculosis status is not required under this section if the child or a person acting on behalf of the child provides the public school district or nonpublic school with documentation showing a

(1) negative result of a PPD skin test administered within the preceding six months;

(2) negative result from an alternative laboratory-approved method administered within the preceding six months for assessing tuberculosis status; or

(3) positive result at any time on the PPD skin test or other alternative laboratory-approved method for assessing tuberculosis status.

(f) A student whose tuberculosis screening outcome obtained under (a) of this section has a positive result shall have a health evaluation by a health care provider. The health care provider shall report the case to the section of epidemiology in the department.

History: Eff. 9/2/82, Register 83; am 2/10/99, Register 149; am 12/29/2013, Register 208

Authority: AS 14.30.045

AS 14.30.065

AS 18.05.040

AS 44.29.020

Resources and References

Conditions Reportable to Public Health Manual
http://dhss.alaska.gov/dph/Epi/Documents/pubs/conditions/ConditionsReportable.pdf

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 respirator.

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 respirator 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.

baseline tuberculosis screening: Screening healthcare workers (HCWs) for latent TB infection and TB disease at the beginning of employment. TB screening includes a symptom screen for all HCWs and 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). In the United States, the currently available IGRAs are the QuantiFERON®-TB Gold (QFT-G) test and the QuantiFERON®-TB Gold in-tube (QFT™) test.

boosting: When nonspecific or remote sensitivity to tuberculin (purified protein derivative [PPD] in the skin test) wanes or disappears with time, subsequent tuberculin skin tests can restore the sensitivity. This is called boosting or the booster phenomenon. An initially limited reaction size is followed by a larger

reaction size on a later test, which can be confused with a conversion or a recent *M. tuberculosis* infection. Two-step testing is used to distinguish new infections from boosted reactions in infection-control surveillance programs, but this method is not recommended for testing contacts.

bronchoscopy: A procedure for examining the lower respiratory tract in which the end of the endoscopic instrument is inserted through the mouth or nose (or tracheostomy) 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.

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 blood assay for *M. tuberculosis* (BAMT) is used for testing, a conversion is a change from a negative to a positive BAMT result over a 2-year period. 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) in the setting in a specified period (numerator) by the number of HCWs 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. 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.

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., 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, or lymph nodes). The presence of extrapulmonary disease does not exclude pulmonary TB disease.

false-negative tuberculin skin test (TST) or blood assay for *M. tuberculosis* (BAMT) result: A TST or BAMT result that is interpreted as negative in a person who is actually infected with *M. tuberculosis*.

false-positive tuberculin skin test (TST) or blood assay for *M. tuberculosis* (BAMT) result: A TST or BAMT 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.

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.

GeneXpert:

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).

high efficiency particulate air (HEPA) filter: A portable or stationary filter that is certified to remove more than 99.97% of particles 0.3 μm 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” is the broader term, and “immunosuppressed” 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.

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 3 months before the symptom onset date (whichever is earlier). The infectious period 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 type of an *ex vivo* test that detects cell-mediated immune response to this cytokine. In the United States, QuantiFERON®-TB Gold (QFT-G) and QuantiFERON®-TB Gold in-tube (QFT™) are the currently available IGRAs.

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 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 chemotherapy.

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-facepiece respirator that is more than 95% efficient at removing 0.3 *µ*m 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**.

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 (NAA): 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. NAA tests for *M. tuberculosis* complex are sensitive and specific; they can accelerate confirmation of pulmonary TB disease.

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.

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.

powered air-purifying respirator (PAPR): A respirator equipped with a tight-fitting facepiece (rubber facepiece) or loose-fitting facepiece (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 facepiece, 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.

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™), QuantiFERON®-TB test (QFT), and QuantiFERON®-TB Gold test (QFT-G): Types of blood assays for *M. tuberculosis* that are *in vitro* cytokine assays that detects 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. In 2005, QFT was replaced by QFT-G, and in 2007 the QFT™ was approved by the FDA. The QFT-G and QFT™ have greater specificity than the original QFT. QFT-G and QFT™ appear to be capable of distinguishing between the sensitization caused by *M. tuberculosis* infection and that caused by bacille Calmette-Guérin vaccination. The QFT™ test has an advantage over the QFT-G test in that the QFT™ allows longer time (3 days) between the blood specimen collection and its arrival at a qualified laboratory. The blood specimen for the QFT-G test must arrive at the laboratory within 12 hours of collection.

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 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, 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. The period for “recent” is

not defined but usually will be briefer than 2 years. Technically, all cases are secondary, in that they originate from other contagious cases.

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. However, specimens suspected to be inadequate should still be processed because positive culture results can still be obtained and might be the only bacteriologic indication of 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).

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.

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 just beneath the surface of the skin (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**.

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).