

ACHA Guidelines

Tuberculosis Screening and Targeted Testing of College and University Students

Purpose

Screening and targeted testing for tuberculosis (TB) is a key strategy for controlling and preventing infection on college and university campuses. Early detection provides an opportunity to promote the health of affected individuals through prompt diagnosis and treatment while preventing potential spread to others. Implementation of a screening and targeted testing program not only addresses this public health concern in campus communities but also contributes to the larger public health goal of reducing the burden of TB in the United States.

The intent of this document is to provide guidelines for screening the incoming student population, targeting those at increased risk for TB testing, and reviewing appropriate follow-up care for students diagnosed with latent TB infection (LTBI) or TB disease.

Definitions

In this document, “screening” refers to the process of identifying persons at high risk for TB infection and disease. Screening is conducted through a questionnaire where the student identifies any risk factors for TB infection and disease. “Testing” refers to the testing procedure for diagnosing LTBI, i.e., the Mantoux tuberculin skin test (TST) or interferon gamma release assay (IGRA).

Risks for exposure to and/or infection with *M. tuberculosis* have been identified through epidemiological and population-based studies (see Table 1). A sample screening questionnaire has been developed based on these risk factors (see Appendix B). It is designed for use by institutions for the incoming student population, in order to appropriately target students at risk for TB who would benefit from testing.

Refer to Table 2 for those factors that place an individual who is infected with TB at higher risk for progressing to active disease. Typically, factors are identified in individuals by health care providers in the clinic setting. Those at risk for exposure should be tested and if positive, are high priorities for treatment.

Whom to Screen

All incoming students should be screened for risk factors for TB through a screening questionnaire. The United States is primarily a low-incidence country, so most U.S.-born incoming students will not have risk factors for TB and will not need TB testing. However, international students arriving from countries or territories with an increased incidence of TB should be tested because this subpopulation has been identified epidemiologically as having a higher incidence of LTBI and an increased risk for developing active TB disease.¹ While all incoming students should be screened, only those students with identifiable risk factors for exposure to TB and/or for TB disease should be tested. Incoming students at low risk should not be tested for TB. Students with a documented previous positive test should not be retested.

High-incidence areas are defined as countries or territories with an annual incidence of TB disease of greater than or equal to 20 cases per 100,000 population. Most countries in Africa, Asia, Central America, Eastern Europe, and South America are included in this group. See Appendix A for a current list of low-incidence countries and territories, as identified by the World Health Organization (WHO) Global Health Observatory.

While national trends indicate a decline in the overall number of TB cases since 1993, active disease transmission continues to occur. It is important to focus on local epidemiology to identify trends in individual states or regions. The epidemiology of TB among foreign-born populations differs considerably from area to area. To tailor TB-control efforts to local needs, TB-control programs should develop epidemiologic profiles to identify groups of foreign-born persons in their jurisdictions who are at higher risk for TB. In 2009, approximately 60% of TB cases in the United States

¹ Centers for Disease Control and Prevention (CDC). Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR November 2005; 54 (No. RR-12):4-5.

TABLE 1: Persons at Higher Risk for Exposure to and/or Infection with *M. tuberculosis*

- Close contacts of persons known or suspected to have active TB disease
- Foreign-born persons from areas that have a high incidence of active TB disease (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia)
- Persons who visit areas with a high prevalence of TB disease, especially if visits are frequent or prolonged
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, long-term care facilities, and homeless shelters)
- Health care workers who serve clients who are at increased risk for active TB disease
- Populations defined locally as having an increased incidence of latent *M. tuberculosis* infection or active TB disease, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol
- Infants, children, and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or active TB disease

Source: Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination. Core Curriculum on Tuberculosis: What the Clinician Should Know: Chapter 1, Table 1.3. Persons at higher Risk for Exposure to and/or Infection with *M. tuberculosis*. 5th edition (2011). <http://www.cdc.gov/tb/education/corecurr/pdf/chapter1.pdf>. Accessed April 11, 2012.

TABLE 2: Persons at Increased Risk for Progression of LTBI to TB Disease

- Persons infected with HIV
- Children younger than 5 years of age
- Persons who were recently infected with *M. tuberculosis* (within the past 2 years)
- Persons with a history of untreated or inadequately treated TB disease, including persons with fibrotic changes on chest radiograph consistent with prior TB disease
- Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation
- Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, or cancer of the head, neck, or lung
- Persons who have had a gastrectomy or jejunioileal bypass
- Persons who weigh less than 90% of their ideal body weight
- Cigarette smokers and persons who abuse drugs and/or alcohol
- Populations defined locally as having an increased incidence of disease due to *M. tuberculosis*, including medically underserved, low-income populations.

Source: Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination. Core Curriculum on Tuberculosis: What the Clinician Should Know: Chapter 2, Table 2.6. Persons at Increased Risk for Progression of LTBI to TB Disease. 5th edition (2011). <http://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf>. Accessed April 11, 2012.

occurred in foreign-born individuals. The majority of U.S. cases among foreign-born individuals are in people from seven countries (Mexico, Philippines, Vietnam, India, China, Haiti, and Guatemala). For a list of high burden countries and their profiles, see the Stop TB Partnership website at www.stoptb.org/countries/tbdata.asp.

Continuing students should be tested only when their activities place them at risk for a new infection or to meet an academic programmatic requirement. While it would be welcomed, no evidence-based data exists that identifies the amount of time spent in a given high-risk country that constitutes significant exposure. Students should discuss the specific travel circumstances with a

health care provider who can determine the appropriate evaluation.²

Activities that may result in increased risk of exposure to TB may include, but are not limited to, volunteering, conducting research, mentoring, studying abroad, traveling, visiting relatives, or employment which may involve close contact with individuals in areas with increased incidence of TB whether domestically or internationally. Sponsors of these programs or health

² Centers for Disease Control and Prevention (CDC). Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. MMWR December 2005; 54 (No. RR-17):4-5.

care providers caring for these students prior to the activity should educate students of this risk and recommend testing 8 to 10 weeks after leaving the high-incidence area.

Health profession students, whether incoming or continuing, should be tested annually.

In the clinical setting, health care providers are encouraged to identify students who are at increased risk of LTBI or TB disease through screening and to test students at risk using tuberculin skin test (TST) or interferon gamma release assays (IGRA) as part of a routine evaluation.

When to Screen and Test

TB screening should occur by questionnaire prior to arrival on campus in conjunction with verification of pre-matriculation immunization requirements. TB testing of high-risk students only should take place no sooner than six months prior to college entrance and should be completed by the second quarter/semester registration.

How to Test

Tuberculin Skin Test (TST)

At the present time, the Mantoux test is the only acceptable TST. To perform this test, inject 0.1 ml of purified protein derivative (PPD) tuberculin containing 5 tuberculin units (TU) intradermally into the volar (inner) surface of either forearm.

While cross-reactivity between PPD and bacillus Calmette-Guerin (BCG) vaccine is possible, a history of BCG vaccination should **not** preclude tuberculin skin testing of students. However, testing with an IGRA, which does not cross-react with BCG, may be preferable to using PPD in students with a history of BCG vaccination, if feasible.

TST can be administered during pregnancy.

If a student has recently received a live virus vaccination, skin testing should be delayed for 4-6 weeks after the student received the vaccination. However, a TST can be performed on the same day as live virus administration without compromising the integrity of the result.

Two-step testing is particularly important and should be considered for the initial skin testing of persons who will be retested periodically, e.g., all health profession students, workers, and volunteers. Two-step testing is more reliable in identifying remote infection (e.g., infection in childhood). If the first test is positive, the person should be considered infected. If the first test is

negative, a repeat test should be administered 1-3 weeks later. If the second test is positive, consider the person infected. If there is documentation of a negative TST within the prior 12 months, only one TST needs to be done, and this is considered the second of the two-step tests.

Interferon Gamma Release Assays (IGRAs)

At the present time, the IGRA method may be used in all circumstances in which the TST is currently used. The U.S. Centers for Disease Control and Prevention (CDC) TB infection control guidelines indicate that IGRAs should be used with caution in immunocompromised patients as this method has not been studied extensively in this group.³

In direct comparisons, the sensitivity of the IGRA is similar to that of TST in infected persons with culture-positive TB. The IGRAs are thought to be more specific than the TST because they do not cross-react to BCG vaccine or to many commonly encountered nontuberculous mycobacteria. IGRAs may be preferred for testing persons who have received BCG and persons unlikely to return for TST reading.⁴

Because many persons who are at high risk for TB infection come from areas of the world for which BCG is routinely used, a task force composed of the CDC, the American Thoracic Society, and the Infectious Diseases Society of America advises that all persons from high incidence countries be regarded as having taken BCG.⁵ Multiple additional recommendations provided address quality control, test selection, and medical management after testing.

Although routine testing with both TST and IGRA is not recommended, there are situations when results from **both** tests may be useful:⁶

- When the initial test is **negative** and
 - high risk for infection, progression to disease, and poor outcome (e.g., persons with HIV) are increased.

³ Centers for Disease Control and Prevention (CDC). Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. MMWR December 2005; 54 (No. RR-17):4-5.

⁴ Centers for Disease Control and Prevention (CDC). Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection – United States, 2010. MMWR 2010; 59 (RR-5):1-25.

⁵ Centers for Disease Control and Prevention (CDC). Core Curriculum on Tuberculosis: What the Clinician Should Know. 5th Edition, 2011.

⁶ Centers for Disease Control and Prevention (CDC). Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection – United States, 2010. MMWR 2010; 59 (RR-5):1-25.

- clinical suspicion for TB disease and confirmation of *M. tuberculosis* infection is desired; in this case having a positive result from the second test as evidence of infection increases detection sensitivity.
- When the initial test is **positive** and
 - additional evidence of infection is required to encourage acceptance and adherence (e.g., in foreign-born persons who attribute a positive TST to prior BCG vaccination).

Two-step testing is not needed with IGRAs. As with TST, IGRA testing should be performed on the same day as, or four weeks after, the administration of a live-virus vaccine.

How to Interpret the TST

The TST should be read 48 to 72 hours after injection of PPD by measuring the transverse diameter of the induration across the forearm, perpendicular to the long axis. Redness or bruising is not measured.

The results are recorded in millimeters (mm) of induration. If no induration is present, "0 mm" is recorded.

Interpretation of the TST depends on both the millimeters of induration and the factors related to risk of exposure to TB disease and risk for progression to TB disease once infected.

>5mm is positive in the following:

- recent contacts of persons with infectious TB disease.
- persons with fibrotic changes on a prior chest x-ray, consistent with past TB disease.
- organ transplant recipients and other immunosuppressed persons (including receiving equivalent of >15 mg/d of prednisone for >1 month.).
- HIV-infected persons.

>10mm is positive in the following:

- recent arrivals to the U.S. (<5 years) from high prevalence areas or who resided in one for a significant* amount of time.
- injection drug users.
- mycobacteriology laboratory personnel.
- residents, employees, or volunteers in high-risk congregate settings.
- persons with medical conditions that increase the risk of progression to TB disease including silicosis,

diabetes mellitus, chronic renal failure, certain types of cancer (leukemias and lymphomas, cancers of the head, neck, or lung), gastrectomy or jejunioileal bypass and weight loss of at least 10% below ideal body weight.

>15mm is positive in the following:

- persons with no known risk factors for TB who, except for certain testing programs required by law or regulation, would otherwise not be tested.⁷

**The significance of the exposure should be discussed with a health care provider and evaluated.*

What to Do When the TST or IGRA Is Positive

Persons with a positive TST or IGRA must undergo chest radiography and medical exam. If any x-ray changes or signs and symptoms of active TB are identified, active TB disease must be excluded.

If the chest x-ray and medical exam are normal, treatment for LTBI should be recommended since this greatly reduces the risk of TB infection progressing to TB disease in the student and serves to reduce the burden of TB in the U.S. HIV testing is recommended for all LTBI patients, unless the patient declines (opt-out screening). Treatment is most important for those with a particularly high risk for progression from latent infection to active disease including individuals who had a TST conversion within two years and those with HIV/AIDS or other clinical conditions associated with suppressed immunity (see Table 2).

Treatment with isoniazid (INH) daily for nine months is the preferred regimen⁸; however, other regimens may be appropriate.⁹ A four-month course of Rifampin is also efficacious. A shorter course using INH plus rifapentine once weekly for three months under directly observed therapy (DOT) or self-administered can be used for select patients.¹⁰

Short course therapy offers a potential advantage for students to complete treatment within a single semester.

⁸ Centers for Disease Control and Prevention (CDC). Latent Tuberculosis Infection: A Guide for Primary Health Care Providers. www.cdc.gov/tb/publications/ltni/treatment.htm

⁹ Centers for Disease Control and Prevention (CDC). Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR 2011. December 9, 2011/60 (48):1650-1653.

¹⁰ Centers for Disease Control and Prevention (CDC). Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR 2018. June 29, 2018 / 67(25):723-726.

Consultation with the local or state health department or an infectious disease specialist is recommended. Note: rifampin should not be used in pregnancy and may reduce the effectiveness of hormonal contraception.

Completion of treatment should be a high priority and should be supported by providing education in the student's primary language, insuring confidentiality, offering incentives to mark treatment milestones, and case management by a culturally competent health care provider to build trust and gain buy-in.

Baseline laboratory monitoring of ALT, AST, and bilirubin during treatment of LTBI is indicated *only* for students

- with a history of liver disorder.
- with a risk of chronic liver disease.
- who regularly use alcohol.
- with HIV infection.
- who are pregnant or up to three months postpartum.

Students with baseline abnormal liver function tests should be monitored at regular intervals with clinical and laboratory evaluation. Testing may be considered on an individual basis, particularly in those taking medications for chronic medical conditions.

All others receiving treatment for LTBI need only monthly review of symptoms to monitor for medication side effects.

Post-treatment follow-up should include providing the student documentation of TST or IGRA results, chest radiograph results, and the dosage and duration of medication treatment. Students who have completed LTBI therapy, as well as those who elected not to take therapy, should be educated regarding signs and symptoms of TB disease and instructed to seek medical care immediately upon developing any of the signs or symptoms of TB.

Additional Resources (*in addition to footnotes*)

ATS/CDC/IDSA. Treatment of Tuberculosis. MMWR June 2003; 52 (No. RR-11).

Francis J. Curry National Tuberculosis Center. TB Program Manual Template.

<https://www.currytbcenter.ucsf.edu/products/tuberculosis-program-manual-template>

Heartland National Tuberculosis Center. Model Tuberculosis Prevention Program for College Campuses. 2nd ed. 2011.

www.heartlandntbc.org/assets/products/model_tb_prevention_program_college_campuses.pdf



APPENDIX A

“Low Incidence” Areas with Estimated or Reported Tuberculosis Incidence, 2017

“Low Incidence” areas are defined as areas with reported or estimated incidence of <20 cases per 100,000 population.

| | | |
|-----------------------------------|----------------------------|--|
| American Samoa | Finland | Saint Kitts and Nevis |
| Andorra | France | Saint Lucia |
| Antigua and Barbuda | Germany | Saint Vincent and the Grenadines |
| Aruba | Greece | Samoa |
| Australia | Grenada | San Marino |
| Austria | Hungary | Saudi Arabia |
| Bahamas | Iceland | Seychelles |
| Bahrain | Iran (Islamic Republic of) | Serbia |
| Barbados | Ireland | Sint Maarten (Dutch part) |
| Belgium | Israel | Slovakia |
| Bermuda | Italy | Slovenia |
| Bonaire, Saint Eustatius and Saba | Jamaica | Spain |
| British Virgin Islands | Japan | Sweden |
| Canada | Jordan | Switzerland |
| Cayman Islands | Lebanon | Syrian Arab Republic |
| Chile | Luxembourg | The Former Yugoslav Republic of Macedonia |
| Cook Islands | Malta | Tokelau |
| Costa Rica | Mauritius | Tonga |
| Croatia | Monaco | Trinidad and Tobago |
| Cuba | Montenegro | Turkey |
| Curacao | Montserrat | Turks and Caicos Islands |
| Cyprus | Netherlands | United Arab Emirates |
| Czechia | New Zealand | United Kingdom of Great Britain and Northern Ireland |
| Denmark | New Caledonia | United States of America |
| Dominica | Norway | US Virgin Islands |
| Egypt | Oman | Wallis and Futuna Islands |
| Estonia | Poland | West Bank and Gaza Strip |
| | Puerto Rico | |

Source: World Health Organization Global Health Observatory, Tuberculosis Incidence 2017.

For future updates, refer to <http://www.who.int/tb/country/en/>.

APPENDIX B

Tool for Institutional Use

Part I: Tuberculosis (TB) Screening Questionnaire (to be completed by incoming students)

Please answer the following questions:

Have you ever had close contact with persons known or suspected to have active TB disease? Yes No

Were you born in one of the countries or territories listed below that have a high incidence of active TB disease? (If yes, please CIRCLE the country, below) Yes No

- | | | | | |
|----------------------------------|---------------------------------------|----------------------------------|--------------------------|------------------------------------|
| Afghanistan | Comoros | India | Namibia | Somalia |
| Albania | Congo | Indonesia | Nauru | South Africa |
| Algeria | Côte d'Ivoire | Iraq | Nepal | South Sudan |
| Angola | Democratic People's Republic of Korea | Kazakhstan | Nicaragua | Sri Lanka |
| Anguilla | Democratic Republic of the Congo | Kenya | Niger | Sudan |
| Argentina | Djibouti | Kiribati | Nigeria | Suriname |
| Armenia | Dominican Republic | Kuwait | Niue | Swaziland |
| Azerbaijan | Ecuador | Kyrgyzstan | Northern Mariana Islands | Tajikistan |
| Bangladesh | El Salvador | Lao People's Democratic Republic | Pakistan | Tanzania (United Republic of) |
| Belarus | Equatorial Guinea | Latvia | Palau | Thailand |
| Belize | Eritrea | Lesotho | Panama | Timor-Leste |
| Benin | eSwatini | Liberia | Papua New Guinea | Togo |
| Bhutan | Ethiopia | Libya | Paraguay | Tunisia |
| Bolivia (Plurinational State of) | Fiji | Lithuania | Peru | Turkmenistan |
| Bosnia and Herzegovina | French-Polynesia | Madagascar | Philippines | Tuvalu |
| Botswana | Gabon | Malawi | Portugal | Uganda |
| Brazil | Gambia | Malaysia | Qatar | Ukraine |
| Brunei Darussalam | Georgia | Maldives | Republic of Korea | Uruguay |
| Bulgaria | Ghana | Mali | Republic of Moldova | Uzbekistan |
| Burkina Faso | Greenland | Marshall Islands | Romania | Vanuatu |
| Burundi | Guam | Mauritania | Russian Federation | Venezuela (Bolivarian Republic of) |
| Cabo Verde | Guatemala | Mexico | Rwanda | Viet Nam |
| Cambodia | Guinea | Micronesia (Federated States of) | Sao Tome and Principe | Yemen |
| Cameroon | Guinea-Bissau | Mongolia | Senegal | Zambia |
| Central African Republic | Haiti | Morocco | Sierra Leone | Zimbabwe |
| Chad | Honduras | Mozambique | Singapore | |
| China | | Myanmar | Solomon Islands | |
| China, Hong Kong SAR | | | | |
| China, Macao SAR | | | | |
| Colombia | | | | |

Source: World Health Organization Global Health Observatory, Tuberculosis Incidence 2017. Countries with incidence rates of ≥ 20 cases per 100,000 population. For future updates, refer to <http://www.who.int/tb/country/en/>.

Have you had frequent or prolonged visits* to one or more of the countries or territories listed above with a high prevalence of TB disease? (If yes, CHECK the countries or territories, above) Yes No

Have you been a resident and/or employee of high-risk congregate settings (e.g., correctional facilities, long-term care facilities, and homeless shelters)? Yes No

Have you been a volunteer or health care worker who served clients who are at increased risk for active TB disease? Yes No

Have you ever been a member of any of the following groups that may have an increased incidence of latent *M. tuberculosis* infection or active TB disease: medically underserved, low-income, or abusing drugs or alcohol? Yes No

If the answer is YES to any of the above questions, [insert your college/university name] requires that you receive TB testing as soon as possible but at least prior to the start of the subsequent semester).

If the answer to all of the above questions is NO, no further testing or further action is required.

* The significance of the travel exposure should be discussed with a health care provider and evaluated.

