Baseline TST; Two-Step Testing; Boosting

Centers for Disease Control and Prevention. ***Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005***. MMWR 2005; 54 (No. RR-17)

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"**TB Screening Procedures for Settings (or HCWs)**
Classified as Low Risk
• All HCWs should receive baseline TB screening upon hire, using two-step TST or a single BAMT to test for infection with *M. tuberculosis*.
• After baseline testing for infection with *M. tuberculosis*, additional TB screening is not necessary unless an exposure to *M. tuberculosis* occurs.
• HCWs with a baseline positive or newly positive test result for *M. tuberculosis* infection (i.e., TST or BAMT) or documentation of treatment for LTBI or TB disease should receive one chest radiograph result to exclude TB disease (or an interpretable copy within a reasonable time frame, such as 6 months). Repeat radiographs are not needed unless symptoms or signs of TB disease develop or unless recommended by a clinician (*39,116*).

TB Screening Procedures for Settings (or HCWs)
Classified as Medium Risk
• All HCWs should receive baseline TB screening upon hire, using two-step TST or a single BAMT to test for infection with *M. tuberculosis*.
• After baseline testing for infection with *M. tuberculosis*, HCWs should receive TB screening annually (i.e., symptom screen for all HCWs and testing for infection with *M. tuberculosis* for HCWs with baseline negative test results).
• HCWs with a baseline positive or newly positive test result for *M. tuberculosis* infection or documentation of previous treatment for LTBI or TB disease should receive one chest radiograph result to exclude TB disease. Instead of participating in serial testing, HCWs should receive a symptom screen annually. This screen should be accomplished by educating the HCW about symptoms of TB disease and instructing the HCW to report any such symptoms immediately to the occupational health unit. Treatment for LTBI should be considered in accordance with CDC guidelines (*39*).

TB Screening Procedures for Settings (or HCWs)
Classified as Potential Ongoing Transmission
• Testing for infection with *M. tuberculosis* might need to be performed every 8–10 weeks until lapses in infection control have been corrected, and no additional evidence of ongoing transmission is apparent.
• The classification of potential ongoing transmission should be used as a temporary classification only. It warrants immediate investigation and corrective steps. After

a determination that ongoing transmission has ceased, the setting should be reclassified as medium risk. Maintaining the classification of medium risk for at least 1 year is recommended.

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Baseline test results 1) provide a basis for comparison in the event of a potential or known exposure to *M. tuberculosis* and 2) facilitate the detection and treatment of LTBI or TB disease in an HCW before employment begins and reduces the risk to patients and other HCWs. If TST is used for baseline testing, two-step testing is recommended for HCWs whose initial TST results are negative (*39,224*). If the first-step TST result is negative, the second-step TST should be administered 1–3 weeks after the first TST result was read. If either 1) the baseline first-step TST result is positive or 2) the first-step TST result is negative but the second-step TST result is positive, TB disease should be excluded, and if it is excluded, then the HCW should be evaluated for treatment of LTBI. If the first and second-step TST results are both negative, the person is classified as not infected with *M. tuberculosis*. If the second test result of a two-step TST is not read within 48–72 hours, administer a TST as soon as possible (even if several months have elapsed) and ensure that the result is read within 48–72 hours (*39*). Certain studies indicate that positive TST reactions might still be measurable from 4–7 days after testing (*225,226*). However, if a patient fails to return within 72 hours and has a negative test result, the TST should be repeated (*42*). A positive result to the second step of a baseline two-step TST is probably caused by boosting as opposed to recent infection with *M. tuberculosis*. These responses might result from remote infections with *M. tuberculosis*, infection with an NTM (also known as MOTT), or previous BCG vaccination. Two-step testing will minimize the possibility that boosting will lead to an unwarranted suspicion of transmission of *M. tuberculosis* with subsequent testing. A second TST is not needed if the HCW has a documented TST result from any time during the previous 12 months (see Baseline Testing for *M. tuberculosis* Infection After TST Within the Previous 12 Months).

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BOX 1. Indications for two-step tuberculin skin tests (TSTs)

Situation	Recommended testing
No previous TST result	Two-step baseline TSTs
Previous negative TST result (documented or not) >12 months before new employment	Two-step baseline TSTs
Previous documented negative TST result ≤12 months before new employment	Single TST needed for baseline testing; this test will be the second-step
≥2 previous documented negative TSTs but most recent TST >12 months before new employment	Single TST; two-step testing is not necessary
Previous documented positive TST result	No TST
Previous undocumented positive TST result*	Two-step baseline TST(s)
Previous BCG† vaccination	Two-step baseline TST(s)
Programs that use serial BAMT,§ including QFT¶ (or the previous version QFT)	See Supplement, Use of QFT-G** for Diagnosing *M. tuberculosis* Infections in Health-Care Workers (HCWs)

* For newly hired health-c are workers and other persons who will be tested on a routine basis (e.g., residents or staff of correctional or long-term–care facilities), a previous TST is not a contraindication to a subsequent TST, unless the test was associated with severe ulceration or anaphylactic shock, which are substantially rare adverse events. If the previous positive TST result is not documented, administer two-step TSTs or offer BAMT. **SOURCES:** Aventis Pasteur. Tuberculin purified protein derivative (Mantoux) Tubersol® diagnostic antigen. Toronto, Ontario, Canada: Aventis Pasteur; 2001. Parkdale Pharmaceuticals. APLISOL (Tuberculin purified protein derivative, diluted [stabilized solution]). Diagnostic antigen for intradermal injection only. Rochester, MI: Parkdale Pharmaceuticals; 2002. Froeschle JE, Ruben FL, Bloh AM. Immediate hypersensitivity reactions after use of tuberculin skin testing. Clin Infect Dis 2002;34:E12–3.
† Bacille Calmette-Guérin.
§ Blood assay for *Mycobacterium tuberculosis*.
¶ QuantiFERON®-TB test.
** QuantiFERON®-TB Gold test.

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Serial Follow-Up of TB Screening and Testing for *M. tuberculosis* Infection

The need for serial follow-up screening for groups of HCWs with negative test results for *M. tuberculosis* infection is an institutional decision that is based on the setting's risk classification. This decision and changes over time based on updated risk assessments should be official and documented. If a serial follow-up screening program is required, the risk assessment for the setting (see TB Risk Assessment Worksheet [Appendix B]) will determine which HCWs should be included in the program and the frequency of screening. Two-step TST testing should not be performed for follow-up testing.

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In a contact investigation, a follow-up TST should be administered 8–10 weeks after the end of exposure (rather than 1–3 weeks later, as in two-step testing). In this instance, a change from a negative TST result to a positive TST result should not be interpreted as a boosted reaction. The change in the TST result indicates a TST conversion, recent exposure, transmission, and infection.

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Booster phenomenon and two-step testing. In certain persons with LTBI, the DTH responsible for TST reactions wanes over time. Repeated TST can elicit a reaction called

boosting in which an initial TST result is negative, but a subsequent TST result is positive. For example, a TST administered years after infection with *M. tuberculosis* can produce a falsenegative result. This TST might stimulate (or boost) the person's ability to react to tuberculin, resulting in a positive result to a subsequent test (including the second step of a twostep procedure) (*36,74,316,342,343*). With serial testing, a boosted reaction on a subsequent TST might be misinterpreted as a newly acquired infection, compared with the falsenegative result from the initial TST. Misinterpretation of a boosted reaction as a new infection with *M. tuberculosis* or TST conversion might prompt unnecessary investigations to find the source case, unnecessary treatment for the person tested, and unnecessary testing of other HCWs. The booster phenomenon can occur in anyone, but it is more likely to occur in older persons, persons with remote infection with *M. tuberculosis* (i.e., infected years ago), persons infected with NTM, and persons with previous BCG vaccination (*39,229,234,344,345*). All newly employed HCWs who will be screened with TST should receive baseline two-step TST upon hire, unless they have documentation of either a positive TST result or treatment for LTBI or TB disease (*39,224*). Any setting might have HCWs at risk for boosting, and a rate of boosting even as low as 1% can result in unnecessary investigation of transmission. Therefore, two-step TSTs are needed to establish a baseline for persons who will receive serial TST (e.g., residents or staff of correctional facilities or LTCFs). This procedure is especially important for settings that are classified as low risk where testing is indicated only upon exposure. A reliable baseline test result is necessary to detect health-care–associated transmission of *M. tuberculosis*. Guidance for baseline TST for HCWs is included in this report (Box 2).

BOX 2. Interpretations of tuberculin skin test (TST) and QuantiFERON®-TB test (QFT) results according to the purpose of testing for *Mycobacterium tuberculosis* infection in a health-care setting

Purpose of testing	TST	QFT
1. Baseline	1. ≥10 mm is considered a positive result (either first- or second-step)	1. Positive (only one-step)
2. Serial testing without known exposure	2. Increase of ≥10 mm is considered a positive result (TST conversion)	2. Change from negative to positive (QFT conversion)
3. Known exposure (close contact)	3. ≥5 mm is considered a positive result in persons who have a baseline TST result of 0 mm; an increase of ≥10 mm is considered a positive result in persons with a negative baseline TST result or previous follow-up screening TST result of ≥0 mm	3. Change to positive

To estimate the frequency of boosting in a particular setting, a four-appointment schedule of TST administration and reading (i.e., appointments for TST administration and reading both TST results) is necessary, rather than the three-appointment schedule (i.e., appointments for the administration of both tests, with reading of the second-step TST result only) (*196*). Two-step testing should be used only for baseline screening, not in contact investigations. In a contact investigation, for persons with a negative TST, a follow-up test should be administered 8–10 weeks after the end of exposure (rather than 1–3 weeks later, as in a two-step TST). In this instance, a change from a

negative to a positive TST result suggests that recent exposure, transmission, and infection occurred and should not be interpreted as a boosted response. After a known exposure in a health-care setting (close contact to a patient or HCW with infectious TB disease), TST results of >5 mm should be considered positive and interpreted as a new infection in HCWs whose previous TST result is 0 mm. If an HCW has a baseline or follow-up TST result of >0 mm but <10 mm, a health-care–associated exposure to *M. tuberculosis,* and an increase in the TST size of >10 mm, the result should be interpreted as the HCW having a TST conversion because of new infection.

BCG vaccination. In the United States, vaccination with BCG is not recommended routinely for anyone, including HCWs or children (*227*). Previous BCG vaccination is not a contraindication to having a TST or two-step skin testing administered. HCWs with previous BCG vaccination should receive baseline and serial skin testing in the same manner as those without BCG vaccination (*233*) (see Supplement, Diagnostic Procedures for LTBI and TB Disease; Box 1). Previous BCG vaccination can lead to boosting in baseline two-step testing in certain persons (*74,231,344–346*). Distinguishing a boosted TST reaction resulting from BCG vaccination (a false-positive TST result) and a TST result because of previous infection with *M. tuberculosis* (true positive TST result) is not possible (*39*). Infection-control programs should refer HCWs with positive TST results for medical evaluation as soon as possible (see Supplement, Diagnostic Procedures for LTBI and TB Disease; Box 2). Previous BCG vaccination increases the probability of a boosted reaction that will probably be uncovered on initial two-step skin testing. For an HCW with a negative baseline two-step TST result who is a known contact of a patient who has suspected or confirmed infectious TB disease, treatment for LTBI should be considered if the follow-up TST result is >5 mm, regardless of BCG vaccination status.

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• **What is boosting?** Boosting is a phenomenon in which a person has a negative TST (i.e., false-negative) result years after infection with *M. tuberculosis* and then a positive subsequent TST result. The positive TST result is caused by a boosted immune response of previous sensitivity rather than by a new infection (false-positive TST conversion). Two-step testing reduces the likelihood of mistaking a boosted reaction for a new infection.

• **What procedure should be followed for a newly hired HCW who had a documented negative TST result 3 months ago at their previous job?** This person should receive one baseline TST upon hire (ideally before the HCW begins assigned duties). The negative TST result from the 3 months preceding new employment (or a documented negative TST result anytime within the previous 12 months) should be considered the first step of the baseline two-step TST. If the HCW does not have documentation of any TST result, the HCW should be tested

with baseline two-step TST (one TST upon hire and one TST placed 1–3 weeks after the first TST result was read).

• **Why are two-step TSTs important for the baseline (the beginning of an HCW's employment)?** If TST is used for TB screening (rather than BAMT), performing twostep TST at baseline minimizes the possibility that boosting will lead to suspicion of transmission of *M. tuberculosis* in the setting during a later contact investigation or during serial testing (false-positive TST conversions). HCWs who do not have documentation of a positive TST result or who have not been previously treated for LTBI or TB disease should receive baseline two-step TST.

• **If a person does not return for a TST reading within 48–72 hours, when can a TST be placed on them again?** A TST can be administered again as soon as possible. If the second step of a two-step TST is not read within 48–72 hours, administer a third test as soon as possible (even if multiple months have elapsed), and ensure that the result is read within 48–72 hours.

• **Do health-care settings or areas in the United States exist for which baseline two-step skin TST for newly hired HCWs is not needed?** Ideally, all newly hired HCWs who might share air space with patients should receive baseline two-step TST (or one-step BAMT) before starting duties. In certain settings, a choice might be offered not to perform baseline TST on HCWs who will never be in contact with or share air space with patients who have TB disease, or who will never be in contact with clinical specimens (e.g., telephone operators in a separate building from patients).

• **In our setting, workers are hired to provide health care in homes, and they are not medically trained. Twostep skin testing is difficult because of the requirement to return for testing and reading multiple times. Can the two-step TST be omitted?** No, ideally, all HCWs who do not have a previously documented positive TST result or treated LTBI or TB disease should receive twostep baseline skin testing in settings that have elected to use TST for screening. BAMT is a single test procedure. Baseline testing for *M. tuberculosis* infection will ensure that TB disease or LTBI is detected before employment begins and treatment for LTBI or TB disease is offered, if indicated.

• **When performing two-step skin testing, what should be done if the second-step TST is not placed in 1–3 weeks?** Perform the second-step TST as soon as possible, even if several months have passed.

• **Should HCWs who report upon hire that they have had a positive TST result or have been previously treated for LTBI or TB disease receive baseline twostep TST when beginning work at a new health-care setting?** Unless the HCW has documentation of a positive TST result or previously treated LTBI or TB

disease, they should usually receive baseline two-step testing before starting duties. If documentation is available of a positive TST result, that result can be considered as the baseline TST result for the HCW at the new setting, and additional testing is not needed. Recommendations for testing HCWs who transfer from one setting to another where the risk assessment might be different are presented (see Use of Risk Classification to Determine Need for TB Screening and Frequency of Screening HCWs).

• **If an HCW has a baseline first-step TST result between 0–9 mm, does a second-step TST need to be placed?** Yes, if the baseline first-step TST result is <10 mm, a second-step TST should be applied 1–3 weeks after the first TST result was read. HCWs who are immunocompromised are still subject to the 10 mm cutoff for baseline two-step testing for surveillance purposes but would be referred for medical evaluation for LTBI using the 5 mm cutoff.