Lunch and Learns

The HIV/STD/TB/Hepatitis Program and the Dakotas AIDS Education and Training Center (DAETC) conduct monthly Lunch and Learn Webinars for health care professionals in North and South Dakota.

Each month a new topic will be held from 12:00 p.m. to 1:00 p.m. CST on the fourth Wednesday of the month.
Continuing Education Credits

Please complete the post-test to receive CEUs for this presentation. You must score at least 70% to receive credit. You may take the post-test up to two weeks after the presentation. Post-test, along with the slides and the recording of this presentation can be found at:

https://www.ndhealth.gov/hiv/Provider/

For questions or comments contact:
Sarah Weninger
701.328.2366
sweninger@nd.gov
By the end of this presentation you will be able to:

- Define who is covered by the new Health Care Personnel guidelines released by the CDC and NTCA.
- Review updated screening, testing and treatment guidelines for Health Care Personnel and identify changes from current guidelines.
- Describe testing options and explain collection and transport of specimens.
- Discuss the Aplisol shortage and discuss recommendations to implement until the shortage is resolved.
CDC and the National TB Controllers Association released updated recommendations for TB screening, testing and treatment of health care personnel on May 17, 2019.
Original guidelines for preventing TB transmission were released in 2005.

Guidelines recommended:
- Baseline screening of Health Care Personnel (HCP)
- Annual testing for HCP in medium and high risk settings or potential for ongoing transmission
BACKGROUND

- HCP increased risk for LTBI and TB disease due to occupational exposures
- Rates of TB disease decreased in the US
- TB incidence rates in HCP were similar to the general population
- Low rates of TST conversion were noted when serial testing performed
- Limitations for serial testing when using TST and IGRA’s
METHODS

• Workgroup formed with representatives from:
  • CDC
  • NTCA
  • State
  • Local Public Health
  • Occupational Health
• Systematic literature review performed
• Updated recommendations developed in December 2017
• Draft of recommendations presented in 2018
Updated Recommendations
• Guidelines outside of scope of HCP screening, testing, treatment and education remain unchanged from 2005 recommendations

• Facility Risk Assessment still recommended
TB screening is defined as a process that includes:

- TB risk assessment
- Symptom evaluation
- TB testing for M. tuberculosis infection (by either IGRA or TST) for health care personnel without documented evidence of prior LTBI or TB disease
- Additional workup for TB disease for health care personnel with positive test results or symptoms compatible with TB disease

This update does not include recommendations for using an IGRA versus a TST for diagnosing LTBI, which have been published elsewhere.
BASELINE SCREENING AND TESTING

All HCP should have a baseline TB screening

- Individual Risk Assessment
- Help guide decisions when interpreting test results

The CDC recommends IGRA be performed for:
- Persons who have received BCG
- Persons from groups that historically have poor rates of returning for TST reading
POSTEXPOSURE SCREENING AND TESTING

After known exposure to a person with potentially infectious TB disease without use of adequate personal protection:

- HCP should have a timely symptom evaluation and additional testing, if indicated.
- Those without documented evidence of prior LTBI or TB disease should have an IGRA or a TST performed.
- Health care personnel with documented prior LTBI or TB disease do not need another test for infection after exposure.
  - These persons should have further evaluation if a concern for TB disease exists.

Those with an initial negative test should be retested 8–10 weeks after the last exposure, preferably by using the same test type as was used for the prior negative test.
In the absence of known exposure or evidence of ongoing TB transmission without LTBI routine serial TB screening or testing not recommended after baseline.

Health care facilities might consider using serial TB screening of certain groups who might be at increased occupational risk for TB exposure.

- Pulmonologists
- Respiratory Therapists
- Microbiology Staff
ANNUAL EDUCATION

- HCP might have risks for TB exposure that are not related to their work in the US
- Might have risks for TB progression after baseline testing that necessitate special consideration
- If these risks are unrecognized, HCP might experience TB disease and transmit TB to patients, coworkers, or other contacts.
- Educate for:
  - Risk factors
  - Signs and symptoms
INDICATORS OF TB RISK

BOX. Indicators of risk* for tuberculosis (TB) at baseline health care personnel assessment?

Health care personnel should be considered to be at increased risk for TB if they answer "yes" to any of the following statements.

1. Temporary or permanent residence (for ≥1 month) in a country with a high TB rate (i.e., any country other than Australia, Canada, New Zealand, the United States, and those in western or northern Europe) or
2. Current or planned immunosuppression, including human immunodeficiency virus infection, receipt of an organ transplant, treatment with a TNF-alpha antagonist (e.g., infliximab, etanercept, or other), chronic steroids (equivalent of prednisone ≥15 mg/day for ≥1 month), or other immunosuppressive medication or
3. Close contact with someone who has had infectious TB disease since the last TB test.

Abbreviations: TNF = tumor necrosis factor.
*Adapted from a tuberculosis risk assessment form developed by the California Department of Public Health. [https://www.cdph.ca.gov/Programs/CID/DCDO/CDPH%20Documents%20Library/TBCB-CA-TB-Risk-Assessment-and-Fact-Sheet.pdf]
HCP with a newly positive test result
- Perform a symptom evaluation
- Chest radiograph

Additional workup might be indicated

HCP with a prior positive TB test and documented normal chest radiograph **do not require** a repeat radiograph unless they are symptomatic or starting LTBI treatment

The local public health department should be notified immediately if TB disease is suspected.
If no prior treatment for LTBI, treatment should be offered and strongly encouraged to complete.

Short-course treatment regimens recommended unless a contraindication exists

HCP with untreated LTBI should be monitored with an annual symptom evaluation

- Detect early evidence of TB disease
- Reevaluate the risks of disease and benefits of treatment
- Educate about signs and symptoms of TB disease
TABLE: Comparison of 2005* and 2019† recommendations for tuberculosis (TB) screening and testing of U.S. health care personnel (HCP)

<table>
<thead>
<tr>
<th>Category</th>
<th>2005 Recommendation</th>
<th>2019 Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (preplacement) screening and testing</td>
<td>TB screening of all HCP, including a symptom evaluation and test (IGRA or TST) for those without documented prior TB disease or LTBI.</td>
<td>TB screening of all HCP, including a symptom evaluation and test (IGRA or TST) for those without documented prior TB disease or LTBI (unchanged); individual TB risk assessment (new).</td>
</tr>
<tr>
<td>Postexposure screening and testing</td>
<td>Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB disease or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure.</td>
<td>Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB disease or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure (unchanged).</td>
</tr>
<tr>
<td>Serial screening and testing for HCP without LTBI</td>
<td>According to health care facility and setting risk assessment. Not recommended for HCP working in low-risk health care settings. Recommended for HCP working in medium-risk health care settings and settings with potential ongoing transmission.</td>
<td>Not routinely recommended (new); can consider for selected HCP groups (unchanged); recommend annual TB education for all HCP (unchanged), including information about TB exposure risks for all HCP (new emphasis).</td>
</tr>
<tr>
<td>Evaluation and treatment of positive test results</td>
<td>Referral to determine whether LTBI treatment is indicated.</td>
<td>Treatment is encouraged for all HCP with untreated LTBI, unless medically contraindicated (new).</td>
</tr>
</tbody>
</table>

Abbreviations: IGRA = interferon-gamma release assay; LTBI = latent tuberculosis infection; TST = tuberculin skin test.

† All other aspects of the Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health Care Settings, 2005 remain in effect, including facility risk assessments to help guide infection control policies and procedures.
2019 RECOMMENDATIONS SUMMARY

CDC AND THE NATIONAL TUBERCULOSIS CONTROLLERS ASSOCIATION RECOMMEND

INDIVIDUAL TB RISK ASSESSMENT

SYMPTOM SCREENING

TB TESTING

FOR HEALTH CARE PERSONNEL UPON HIRE

• NO routine serial TB testing in the absence of a known exposure or ongoing transmission
• Encouragement of treatment for all HCP with untreated LTBI, unless treatment is contraindicated
• Annual symptom screening for HCP with untreated LTBI
• Annual TB education of all HCP
CDC Health Advisory – Aplisol Shortage

June 6, 2019
Nationwide Shortage of Tuberculin Skin Test Antigens: CDC Recommendations for Patient Care and Public Health Practice

Summary
The Centers for Disease Control and Prevention (CDC) is expecting a 3 to 10 month wide-variation shortage of APLISOL®, a product of Par Pharmaceutical Co. APLISOL® is one of two purified-protein derivative (PPD) tuberculin antigens that are licensed by the United States Food and Drug Administration (FDA) for use in performing tuberculin skin tests. The manufacturer notified CDC that they anticipate a supply interruption of APLISOL® 5mL (50 tests) beginning in May 2019, followed by a supply interruption of APLISOL® 1mL (10 tests) in November 2019. The expected shortage of APLISOL® 1mL (10 tests) could occur before November 2019, if demand increases before then. The 3-10 month timeframe for the nationwide shortage is the manufacturer’s current estimate and is subject to change.

To monitor the status of this supply interruption, visit FDA’s “Center for Biologics Evaluation and Research-Regulated Products: Current Shortages” webpage: https://www.fda.gov/center-for-biologics-safety-availability/biologics/ober-regulated-products-current-shortages

Background
Two types of immunological methods are used for detecting Mycobacterium tuberculosis infection: tuberculin skin tests (TSTs) and interferon-gamma release assay (IGRA) blood tests. TSTs and IGRA are used for diagnosing latent TB infection and may aid in diagnosing TB disease. Additional evaluation and testing is necessary to distinguish between latent TB infection and TB disease, and to determine the correct treatment (1). When findings, such as chest radiography and mycobacterial cultures, are sufficient for confirming or excluding the TB diagnosis, the results from a TST or an IGRA blood test might not be needed (1). Most TB cases in the United States are diagnosed with a set of findings including results from one of these tests.

Two FDA-approved PPD tuberculin antigens are available in the United States for use in performing TSTs: TUBERSOL® and APLISOL®. In controlled studies, the concordance between the two products is high (2).

When TB disease is strongly suspected, specific treatment should be started regardless of results from TST or an IGRA blood test (2,4).

Recommendations
CDC recommends three general approaches to prevent a decrease in TB testing capability because of the anticipated shortage of APLISOL®:
- Substitute IGRA blood tests for TSTs. Clinicians who use the IGRA blood tests should be aware that the criteria for test interpretation are different from the criteria for interpreting TSTs (3).
- Substitute TUBERSOL® for APLISOL® for skin testing. In cross-sectional studies, the two skin test products give similar results for most patients.
- Prioritize allocation of TSTs, in consultation with state and local public health authorities. Prioritization might require the deferral of testing some persons. CDC recommends testing only for persons who are at risk of TB (5-7). High-risk groups for TB infection include:
  - People who are recent contacts exposed to persons with TB disease.
  - People born in or who frequently travel to countries where TB disease is common.
  - People who currently or used to live in large group settings, such as homeless shelters or correctional facilities.
  - People with weaker immune systems, such as those with certain health conditions or taking certain medications that may affect immunity; and
  - Children, especially those under age 5, if they are in one of the risk groups noted above.

While overall test concordance is high, switching between PPD skin test products or between TSTs and blood tests in serial testing may cause apparent conversions of results from negative to positive or reversions from positive to negative. This may be due to inherent inter-product or inter-method discordance, rather than change in M. tuberculosis infection status (8). Clinicians should assess test results based on the person’s likelihood of infection and risk of progression to TB disease, if infected (1).

In settings with a low likelihood of TB exposure, the deferral of routine serial testing should be considered in consultation with public health and occupational health authorities. Annual TB testing of healthcare personnel is not recommended unless there is a known exposure or ongoing transmission (8).
CDC RECOMMENDATIONS

CDC recommends three general approaches to prevent a decrease in TB testing capability because of the expected shortage of APLISOL®.

▪ Substitute IGRA blood tests for TSTs. Clinicians who use the IGRA blood tests should be aware that the criteria for test interpretation are different from the criteria for interpreting TST’s.

▪ Substitute TUBERSOL® for APLISOL® for skin testing. In cross-sectional studies, the two skin test products give similar results for most patients.

▪ Prioritize allocation of TSTs, in consultation with state and local public health authorities.
  ▪ Prioritization might require the deferment of testing some persons.
  ▪ CDC recommends testing only for persons who are at risk of TB. High-risk groups for TB infection include:
    ▪ People who are recent contacts exposed to persons with TB disease
    ▪ People born in or who frequently travel to countries where TB disease is common
    ▪ People who currently or used to live in large group settings, such as homeless shelters or correctional facilities
    ▪ People with weaker immune systems, such as those with certain health conditions or taking certain medications that may alter immunity
    ▪ Children, especially those under age 5, if they are in one of the risk groups noted above.
MEMO

TO: Partners in Tuberculosis Prevention & Control

FROM: Dee Pritchett, Tuberculosis Controller, Division of Disease Control
       Christie Massen, Director, Division of Microbiology

DATE: 17 June 2019

RE: Restriction on the Release of PPD from NDDoH Supply

In response to the announced nationwide shortage of APUSOL®, a product of Par Pharmaceuticals, the North Dakota Department of Health (NDoH) has learned from other jurisdictions that the procurement of TUBERSOL® is also becoming increasingly difficult. TUBERSOL® is the FDA approved purified protein derived test (PPD) routinely supplied by NDOH for the purpose of testing for tuberculosis. While not in official shortage, it is expected that due to the high demand for TUBERSOL® in the absence of APUSOL®, TUBERSOL® will be in restricted availability soon. In preparation, NDOH will no longer be delivering orders of PPD for routine screening of tuberculosis. The current state supply of TUBERSOL® will be reserved for the screening of tuberculosis exposed individuals 5 years and younger in which phlebotomy can more difficult for or children under the age of 2 in which interferon-gamma release assay (IGRA) tests are not recommended.

It is strongly suggested that for those over the age of 5 to receive an IGRA blood test in place of a tuberculin skin test (TST). The North Dakota Department of Health, Division of Microbiology, performs these tests daily with results available within 3 days. The cost of this test is $35. For those who have contracts with NDDoH for Tuberculosis Surveillance activities, the costs of these tests are billable to those awards for persons at high-risk for TB infection.

For questions related to specimen collection and submission, please contact Kristie Schwarzkopf at 701.328.6272 or at kschwarzkopf@nd.gov.

For questions related to tuberculosis infection and screening, please feel free to contact Dee Pritchett at 701.328.2377 or at dpritchett@nd.gov.

<table>
<thead>
<tr>
<th>All Settings</th>
<th>All Groups</th>
<th>Do NOT Administer TSTs to persons with a documented previous history of positive TST, IGRA or TB Disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correctional Facilities</td>
<td>Residents</td>
<td>At Time of Admission:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conduct TB Symptom Screen.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Perform TB Screening Test using IGRA. If IGRA not available, administer one TST.</td>
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<tr>
<td></td>
<td></td>
<td>• If one TST administered, defer second step TST until shortage resolves.</td>
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<tr>
<td></td>
<td></td>
<td>• If unable to obtain any PPD, defer both TSTs until shortage resolves.</td>
</tr>
<tr>
<td>Annual Screening: Conduct TB Symptom Screen. Perform TB Screening Test using IGRA. If IGRA not available, defer annual TB in the absence of TB symptoms until shortage resolves. The testing of residents is a higher priority than testing employees.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boarding Care/Nursing Homes</td>
<td>Residents</td>
<td>At Time of Admission:</td>
</tr>
<tr>
<td></td>
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<td>• Conduct TB Symptom Screen. Perform TB Screening Test using IGRA. If IGRA not available, administer one TST.</td>
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</tr>
<tr>
<td>Health Care Settings</td>
<td>Employees</td>
<td>At Time of Hire:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conduct TB Symptom Screen.</td>
</tr>
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<tr>
<td>All Settings</td>
<td>Contact Investigations</td>
<td>At Time of Admission:</td>
</tr>
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<td>• Conduct TB Symptom Screen.</td>
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<tr>
<td></td>
<td></td>
<td>• Consult with NDDoH for guidance in identifying who should be included in contact testing.</td>
</tr>
<tr>
<td>Public Health</td>
<td>Class B and Refugee Health Assessments</td>
<td>At Time of Admission:</td>
</tr>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>• Two-step testing is not indicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Conduct other testing and screening as medically indicated.</td>
</tr>
<tr>
<td>Clinical Practice</td>
<td>Asymptomatic adults at increased risk for TB infection</td>
<td>USPSTF recommends all adults at increased risk for TB infection be screened for TB infection. These groups include: persons born in or who are former residents of countries with increased prevalence of TB; persons who live in, or have lived in, high-risk congregate settings (e.g., homeless shelters and correctional facilities).</td>
</tr>
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<td></td>
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</table>
Laboratory Testing using Quantiferon
Collection, Processing and Transport
QUANTIFERON® TB GOLD PLUS

- 4th generation testing
- Cell-mediated immune response
- More specific than TST
- Unaffected by prior vaccination
Antigens in the 4 tubes simulate tb mycobacterial proteins in the body

- ESAT-6 and CFP-10
- Absent form BCG strains
- Absent from most non-tuberculosis mycobacteria except M. kansasii, M. szulgai and M. marinum
QFT-Plus cannot distinguish between active and latent TB infection.

Results should be used in conjunction with a medical evaluation and chest x-ray.
QFT-PLUS

3 Stage test

- Collection: Lithium Heparin or QFT collection tubes
- Incubation: 16-24 hours
- Analyze
OPTION 1: COLLECT IN 6ML LITHIUM HEPARIN NO GEL TUBE

Collect 6ml in Lithium Heparin NO GEL tube
Label Tube
Mix Well
Put in 2-8°C storage
Transport to Lab within 48hrs
Lab begins the process
OPTION 2: DIRECT COLLECTION INTO QFT-PLUS TUBES

- Collect 1.2ml in Nil, TB1, TB2, Mit tube
- Label each tube and Mix Well
- Transport to incubator within 16 hours
- Remix Well
- Incubate Upright for 16-24 hours
- Spin and refrigerate

Label each tube and Mix Well
Transport to incubator within 16 hours
Remix Well
Incubate Upright for 16-24 hours
Spin and refrigerate
LABELLING SPECIMEN

- All samples must be received with 2 unique identifiers that match the test requisition
- i.e., Patient Name
- i.e., Patient Date of Birth
- Date and time of draw is recommended on either tube or slip
SHIPPING

- If samples are not incubated must be to NDDoH lab within 16 hours
- Lithium Heparin No Gel Room temp: to lab within 12 hours
- Lithium Heparin No Gel Refrigerated: to lab within 48 hours
- Quantiferon TB Gold Collection set incubated and spun: 28 days
SHIPPING METHODS

- FedEx-overnight
- UPS
- US Mail
- NDDoH lab courier service
- Vehicle service to the lab
RESULTS

- **Positive:** M.
  
  Tuberculosis infection likely diagnosis which is made in conjunction with epidemiological history, current medical status and diagnostic evaluation.
RESULTS

- **Negative**: M. Tuberculosis infection NOT likely
RESULTS

- Indeterminate: Likelihood of M. Tuberculosis infection cannot be determined
SPECIAL NOTES

- Lab Can not receive non-incubated samples on Friday
- Lab Hours: Monday-Friday 8:00am-5:00pm excluding State holidays
- Any questions please contact;
  - Kristie Schwarzkopf, 701.328.6272
RESOURCES

- Tuberculosis CDC Website - https://www.cdc.gov/tb/default.htm
- Updated Screening, Testing and Treatment Recommendations - https://www.cdc.gov/mmwr/volumes/68/wr/mm6819a3.htm?s_cid=mm6819a3_w
- Aplisol Shortage HAN - https://emergency.cdc.gov/han/HAN00420.asp
QUESTIONS
THANK YOU

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Kristie Schwarzkopf | Immunology/Virology Program Manager | kschwarzkopf@nd.gov | 701-328-6283

Kristin Rounds | TB Controller | kristin.rounds@state.sd.us | 605.773.4784
Ashley Klatt | Nurse Consultant | Ashley.klatt@state.sd.us | 605.882.5097
• Thank You to Our Speaker!

  Dee Pritschet | TB Controller | djpritschet@nd.gov | 701-328-2377
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• CEU: www.ndhealth.gov/HIV/Provider

• Next Lunch and Learn: August 28th at 12pm CT