TB! Or not TB?

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TB Nurse Consultant
Virginia Department of Health
Agenda

- TB Epi
- Overview of TB vs. LTBI
- TB diagnostics
- Reporting requirements
- Screening and testing of HCP
Who is the VDH TB Program?

DCE Director
Jasie Hearn

Admin Support
Deborah Clayton

Surveillance Team
Laura Young
Jane Tingley
Leah Breitung
Donna Asby-Green

TB Manager
Marshall Vogt

Nurse Consultants
Amanda Khalil
Adwoa Sam

Central Office in Richmond > Office of Epidemiology > Division of Clinical Epidemiology > TB Program
TB AND LATENT TB INFECTION
EPIDEMIOLOGY
### Quick pause

<table>
<thead>
<tr>
<th>Definition</th>
<th>Acronym</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>TB</td>
</tr>
<tr>
<td>Latent TB Infection</td>
<td>LTBI</td>
</tr>
<tr>
<td>Interferon Gamma Release Assay</td>
<td>IGRA</td>
</tr>
<tr>
<td>Tuberculin Skin Test</td>
<td>TST</td>
</tr>
</tbody>
</table>
Global Tuberculosis Incidence

- 2020 → 10 million with TB → 5.8 million reported
- Until COVID-19, TB leading cause of death from a single infectious agent
- 8 countries have 2/3 of TB:
  - India
  - China
  - Indonesia
  - Philippines
  - Pakistan
  - Nigeria
  - Bangladesh
  - South Africa
- 1 in 4 people have LTBI

Tuberculosis in the United States

Rate = 2.4

Total number of reported TB cases, 2011–2021

*Based on provisional NTSS data as of 2.9.22
Tuberculosis in Virginia

Tuberculosis Cases, Virginia, 2012-2021

Number of Cases

Year


234 179 198 212 203 204 205 191 168 161

Rate = 1.9
Country of Birth of Tuberculosis Cases, Virginia, 2021

- U.S.: 23 cases
- Afghanistan
- Philippines
- India
- Ethiopia
- Vietnam

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>6624</td>
</tr>
<tr>
<td>2020</td>
<td>5520</td>
</tr>
<tr>
<td>2021</td>
<td>10591</td>
</tr>
<tr>
<td>2022</td>
<td>1151</td>
</tr>
</tbody>
</table>
LTBI Cases by Case Status, Virginia, 2019-2021

- **2019**:
  - Suspect: 6070
  - Confirmed: 554

- **2020**:
  - Suspect: 5233
  - Confirmed: 287

- **2021**:
  - Suspect: 10318
  - Confirmed: 273
LTBI Case Distribution by Region, Virginia, 2019-2021
Burden of latent TB infection (LTBI) in the U.S.

- CDC estimates 13 million people in the United States have LTBI.
- Without treatment, about 10% of these people will develop TB disease.
- Diabetes! 3 fold increased likelihood of progression to active disease!
- Fortunately, treatment for LTBI is 90% effective in preventing activation of TB disease.

LTBI can also be called TB infection (TBI).
IS IT TB OR LTBI?
Two TB-related conditions

**LTBI**
- Do not feel sick, do not have symptoms, cannot spread TB bacteria to others
- Can have LTBI for years
- TB bacteria in body is alive but inactive
- Can develop into active disease

**Active Disease**
- If TB bacteria become active and multiply, LTBI can turn into active disease
## LTBI vs. active disease

<table>
<thead>
<tr>
<th>LTBI</th>
<th>Active Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubercle bacilli in the body</td>
<td></td>
</tr>
<tr>
<td>Tuberculin skin test or IGRA usually positive</td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>Symptoms</td>
</tr>
<tr>
<td>Chest x-ray (CXR) normal or abnormal but not consistent with TB</td>
<td>Chest x-ray usually abnormal</td>
</tr>
<tr>
<td>Not infectious</td>
<td>Often infectious (sputum)</td>
</tr>
<tr>
<td>Should consider preventive treatment</td>
<td>Needs treatment</td>
</tr>
</tbody>
</table>
Symptoms and sites of active disease

**General symptoms:**
fever, weight loss, loss of appetite, fatigue and night sweats

**Pulmonary disease**
cough, SOB, chest pain, hemoptysis

Symptoms vary dependent on the site

Laryngeal TB is most contagious
The spectrum of TB → infection to disease

- Infection eliminated
  - With innate immune response*
  - Or
  - With acquired immune response

Latent TB infection

Subclinical TB disease

Active TB disease

Mycobacterium tuberculosis

Lung

Heart

Granuloma

<table>
<thead>
<tr>
<th>Test</th>
<th>TST</th>
<th>IGRA</th>
<th>Culture</th>
<th>Sputum smear</th>
<th>Infectious</th>
<th>Symptoms</th>
<th>Preferred treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Positive</td>
<td>Intermittently positive</td>
<td>Usually negative</td>
<td>Sporadically</td>
<td>Mild to severe</td>
<td>Multidrug therapy</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Yes</td>
<td>Yes</td>
<td>Multidrug therapy</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Usually negative</td>
<td>Positive or negative</td>
<td>Mild or none</td>
<td>Preventive therapy</td>
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<tr>
<td>Negative</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Sporadically</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Mild or none</td>
<td>Mild to severe</td>
<td>Mild to severe</td>
<td>None</td>
</tr>
</tbody>
</table>

DOI: 10.1038/nrdp.2016.76 Nature Reviews | Disease Primers
TB Spreads Through the Air

TB spreads from person to person when someone with contagious TB coughs, speaks, or sings.

TB is NOT spread by

- toothbrush
- lips
- handshake
- toilet
- eating and drinking
## Treatment

### LTBI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Treatment Length</th>
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</thead>
<tbody>
<tr>
<td>Isoniazid/Rifapentine (3HP)</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Rifapmin (4R)</td>
<td>4 months</td>
</tr>
<tr>
<td>Isoniazid/Rifampin (3HR)</td>
<td>3 months</td>
</tr>
<tr>
<td>Isoniazid (6H or 9H)</td>
<td>6 or 9 months</td>
</tr>
</tbody>
</table>

### Active Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Treatment Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>4 months</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>6 months</td>
</tr>
<tr>
<td>So many others!</td>
<td>9 months</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>12 months</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>18 months</td>
</tr>
<tr>
<td>Linezolid</td>
<td>+</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td></td>
</tr>
<tr>
<td>Pretomanid...</td>
<td></td>
</tr>
</tbody>
</table>
TB DIAGNOSTICS
Two types of tests to diagnose TB infection

TB BLOOD TEST

OR

TB SKIN TEST
Tuberculin skin test (TST)

- PPD (purified protein derivative) the solution used in testing
- Stimulates a delayed-type hypersensitivity response mediated by T lymphocytes
- Induration NOT erythema
- Must be done in conjunction with TB risk assessment
IGRA (Interferon Gamma Release Assay)

- Measure T cell release of interferon-gamma following stimulation by TB-specific antigens
- Does **not** cross react with BCG vaccine
- Reflects prior contact with *M. tuberculosis* and a few other Mycobacteria
  - *M. kansasii*
  - *M. marinum*
  - *M. szulgai*
  - *M. gordonae*
  - *M. fulvacin*
- T-SPOT or QuantiFERON TB Gold Plus (QFT)
- Built in measure of immune function
T-SPOT

- Drawn in a single lithium heparin tube
- Interferon-gamma (IFN) is captured and presented as spots
- Results are interpreted by subtracting the spot count in the NIL control from the spot count in Panels A and Panels B
  - Positive ≥ 8 spots
  - Borderline 5, 6, 7 spots
  - Negative ≤ 4 spots
  - Invalid
QFT

- Can be drawn in single tube
- Total measure of IFN released
- Results
  - Positive result
    - Mitogen ≥0.50 & Nil ≤8.0
    - TB1 or TB2 minus Nil = >0.35
  - Negative result
    - Mitogen ≥0.50 & Nil ≤8.0
    - TB1 or TB2 minus Nil = <0.35
  - Indeterminate result
    - Mitogen <0.50 or Nil >8.0
    - Decrease immune status
    - Incorrect handling/incubation
TST & IGRA

Do not differentiate between latent or active disease!

Live vaccines can interfere with both the TST and the IGRA
Imaging

- Nodules
- Consolidation
- Cavities
- Pleural effusion
- Lymphadenopathy
- Volume Loss
- Miliary TB
- Enlarged cardiac shadow
Sputum

Generated with a deep productive cough

Thick, Mucopurulent

Hemoptysis (Bloody Sputum)

Watery (acceptable if induced)

Salivary
Sputum Collection Guide

1. Drink water before bed
2. In morning, rinse mouth with filtered water
3. Take slow, deep breaths x 3
4. Inhale then cough hard to produce sputum
5. Spit sputum into tube
6. Provide at least 5mL and tightly close container
7. Label and refrigerate

Sputum

- 3 specimens
- 8 hours apart
- Early morning preferred
- Observed
- Induction
Fluorochrome stain for acid fast bacilli (AFB)

- **M. tuberculosis** or nontuberculous mycobacteria (NTM)
- Lacks sensitivity compared to culture
- Negative result does not rule out mycobacterial infection

- Cannot determine if AFB are live or dead
Smear results

- Quick turnaround (1-2 days)
- Negative
- Positive - with quantification based on the number of AFB seen per field
  - 1+ Rare
  - 2+ Few
  - 3+ Moderate
  - 4+ Many
- 1-2 acid fast bacilli seen - basically an indeterminate result
Nucleic acid amplification (NAA) / polymerase chain reaction (PCR)

Advantages
- Rapid (2-3 hours)
- Direct from clinical specimen
- Increased sensitivity over AFB smear

Disadvantages
- Detects non-viable *M. tb*
- Negative test does not exclude possibility of isolating *M. tb* from culture
- Unsure how long *M. tb* can be detected even after treatment completion

1. In house (DCLS) developed PCR
2. FDA approved GeneXpert
   - Also detects rpoB gene mutations
Quick check

1. Test for infection → IGRA or TST
2. AFB smear
   - Typically on sputum, can be on other specimens
   - Results in 1-2 days
   - Gauge of infectiousness
3. NAA/PCR
   - Molecular detection of TB
   - Done right after the AFB smear
   - Assists with diagnosis
4. Next up....
Culture = gold standard for TB diagnosis

LJ: solid media  

MGIT: liquid media
MTBC takes up to 21 days or more to grow
Identifying growth

Old DCLS method
DNA probe
- Uses complimentary DNA to detect specific species of mycobacteria
- Does not amplify DNA; only detects presence or absence

New DCLS method
Real-time PCR
- Same one used earlier on in testing, just a slightly different process!
- Simultaneous amplification and detection of MTBC and MAC (M. avium) DNA
What can we treat this TB with?

Antimycobacterial susceptibility testing (AST) aka drug susceptibility testing (DST)

- 4-13 day qualitative test
- Based on the growth of the MTBC isolate in the presence of a drug vs. growth in the absence of the drug

Panel
- Isoniazid (low)
- Isoniazid (high)
- Rifampin
- Pyrazinamide
- Ethambutol
- Moxifloxacin

Coming soon!
Resistance?

Any resistance triggers CDC testing

- CDC can run
  - Growth based susceptibilities
  - Molecular Detection of Drug Resistance (MDDR)
What’s reportable?

1. Presumptive & confirmed TB disease
   • Rapid reportable = immediately

2. TB infection (LTBI)
   • Within 3 days

3. Contact investigation activities

TB SCREENING AND TESTING OF HEALTHCARE PERSONNEL
Screening and testing - healthcare personnel (HCP)

- Updated guidance released in May of 2019
- Supplements: Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in healthcare settings (2005)
Companion document

- Expands on, provides clarifications, explanations, and considerations beyond the 2019 recommendations
- Strategies for implementation

**ACOEM GUIDANCE STATEMENT**

*Tuberculosis Screening, Testing, and Treatment of US Health Care Personnel*

*ACOEM and NTCA Joint Task Force on Implementation of the 2019 MMWR Recommendations*

Wendy Thanassi, MD, MA, Amy J. Behrman, MD, Randall Reves, MD, Mark Russi, MD, MPH, Melanie Swift, MD, MPH, Jon Warkentin, MD, MPH, Ryo Miyakawa, MD, Donna Wegener, MA, Lawrence Budnick, MD, MPH, Ellen Murray, RN, PhD, Ann Scarpita, BSN, MPH, Bobbi Jo Hurst, MBA, Sarah Foster-Chang, DNP, ANP-BC, Trini Mathew, MD, MPH, MaryAnn Gruden, MSN, COHN-S/CM, Julie Higashi, MD, PhD, and Thomas Warner Hudson III, MD
Healthcare worker vs. healthcare personnel

- Healthcare personnel (HCP) replaces healthcare worker
- Companion Document:
  - All paid and unpaid, part-time, temporary, contract, student and full-time persons working in healthcare settings.
- Suggested list - Appendix 2
A shift in focus

From:
Routine serial testing

To:
Improving education
Increasing LTBI treatment

Why?

- Annual conversion rates of <1% in HCP
- Low TB incidence rates among HCP
  - 2.5 per 100,000 in HCP vs. 3.0 per 100,000 in general population
- 80% of active TB cases reported are reactivations
4 major areas of recommendation

1. Baseline (preplacement) screening and testing
2. Postexposure screening and testing
3. Serial screening and testing for HCP without LTBI
4. Evaluation and treatment of HCP with positive test results
1. Baseline (preplacement) screening and testing

Before starting a new job in a health care setting, all workers and volunteers should receive:

- TB individual risk assessment
- Symptom screening
- TB test

Health Care Personnel (HCP)
Baseline Individual TB Risk Assessment

HCP should be considered at increased risk for TB if any of the following statements are marked “Yes”:

- Temporary or permanent residence of ≥1 month in a country with a high TB rate
  - Any country other than the United States, Canada, Australia, New Zealand, and those in Northern Europe or Western Europe
  - YES  □
  - NO  □

- OR

- Current or planned immunosuppression, including human immunodeficiency virus (HIV) infection, organ transplant recipient, 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
  - YES  □
  - NO  □

- OR

- Close contact with someone who has had infectious TB disease since the last TB test
  - YES  □
  - NO  □
2. Post exposure screening and testing

- Initiate a contact investigation (CI) any time a potentially infectious case is identified.
  - Exposed HCP, staff members, and other contacts
- **Notify and work with your local health department**
- Characteristics of the exposure dictate the timing and extent of the CI activities
  - Risk and exposure assessment
  - Symptom screen
  - Test results
### Factors affecting transmission

**TABLE 2. Factors that Affect Risk of TB Transmission to Health Care Personnel (HCP)**

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Environmental Factors</th>
<th>Time and Intensity of Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early identification of possible TB disease of respiratory tract</td>
<td>Isolation room under negative air pressure</td>
<td>Risk of transmission is directly proportional to time and intensity of exposure</td>
</tr>
<tr>
<td>Early/prompt transfer of patient into respiratory isolation</td>
<td>Removal of infectious droplet nuclei by adequate air exchanges with exhaust to outside air</td>
<td>Short exposure duration</td>
</tr>
<tr>
<td>Early initiation of effective anti-TB regimen</td>
<td>Use of adequate ultraviolet germicidal irradiation (UVGI)</td>
<td>Infrequent exposure</td>
</tr>
<tr>
<td>Effective antibiotic treatment of 3 days or more</td>
<td>Employee using appropriate personal protective equipment (PPE) (N95, powered air-purifying respirator [PAPR], or equivalent)</td>
<td>Absence of close physical contact</td>
</tr>
<tr>
<td>Patient is not coughing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical mask is worn by patient</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Factors that Increase Risk for TB Transmission to HCP**

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Environmental Factors</th>
<th>Time and Intensity of Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect, lack of, or short duration of TB treatment</td>
<td>Sharing small, enclosed spaces</td>
<td>Prolonged cumulative duration of exposure</td>
</tr>
<tr>
<td>High concentrations of acid-fast bacillus (AFB) on sputum smear</td>
<td>Inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplets</td>
<td>Frequent exposure</td>
</tr>
<tr>
<td>Presence of cough</td>
<td>Recirculation of air containing infectious droplet nuclei</td>
<td>Prolonged close physical proximity</td>
</tr>
<tr>
<td>Cavitation on CXR</td>
<td>Inadequate cleaning and disinfection of medical equipment</td>
<td>Intense exposure (eg, conducting aerosol-generating procedures)</td>
</tr>
<tr>
<td>Oropharyngeal or laryngeal TB</td>
<td>Improper procedures for handling specimens</td>
<td></td>
</tr>
<tr>
<td>Failure to cover the mouth and nose while coughing (or not wearing a mask)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undergoing cough-inducing or aerosol-generating procedures (eg, bronchoscopy, sputum induction, autopsy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture or NAAT + regardless of AFB smear positivity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Partially adapted from Centers for Disease Control and Prevention.
Conducting postexposure screening and testing

- Exposure definition - includes “without the use of adequate personal protection”
- Use IGRA or TST
- At least one test 8-10 weeks after exposure
- Documented prior LTBI
  - Do not need IGRA/TST
  - Rule out active TB
Facility risk assessment and classification

Appendix 1. Facility Risk Assessment

Portions from the 2005 MMWR CDC Guidelines Appendix B: Tuberculosis (TB) Risk Assessment Worksheet
Suggested updates to Reflect the 2019 MMWR CDC/NTCA Recommendations are in bold underlined text.

The 2019 MMWR CDC/NTCA Recommendation states: “Recommendations from the 2005 CDC Guidance that are outside the scope of healthcare personnel screening, testing, treatment, and education remain unchanged; this includes continuing annual facility risk assessments for guiding infection control policies and procedures.”

Recommendations from the 2005 CDC Guidance that are outside of the scope of healthcare personnel screening, testing, treatment and education remain unchanged: this includes continuing annual facility risk assessments for guiding infection control policies and procedures. Ensure review of environmental and administrative controls.
Local data - rate tables

<table>
<thead>
<tr>
<th>City/County</th>
<th>2020 Pop*</th>
<th>2017 Cases</th>
<th>2017 Rate</th>
<th>2018 Cases</th>
<th>2018 Rate</th>
<th>2019 Cases</th>
<th>2019 Rate</th>
<th>2020 Cases</th>
<th>2020 Rate</th>
<th>2021 Cases</th>
<th>2021 Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALEXANDRIA DISTRICT</td>
<td>158,726</td>
<td>10</td>
<td>6.4</td>
<td>11</td>
<td>6.9</td>
<td>9</td>
<td>5.6</td>
<td>7</td>
<td>4.4</td>
<td>7</td>
<td>4.4</td>
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<tr>
<td>ARLINGTON DISTRICT</td>
<td>240,119</td>
<td>16</td>
<td>7.0</td>
<td>13</td>
<td>5.5</td>
<td>11</td>
<td>4.6</td>
<td>8</td>
<td>3.4</td>
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<td>23,429</td>
<td>1</td>
<td>4.1</td>
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<td>1</td>
<td>4.2</td>
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<td>Fairfax County</td>
<td>1,150,847</td>
<td>73</td>
<td>6.4</td>
<td>68</td>
<td>5.9</td>
<td>64</td>
<td>5.6</td>
<td>50</td>
<td>4.4</td>
<td>49</td>
<td>4.3</td>
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<td>Falls Church City</td>
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<td>0.0</td>
<td>1</td>
<td>6.8</td>
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<tr>
<td>FAIRFAX DISTRICT</td>
<td>1,188,907</td>
<td>74</td>
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<td>68</td>
<td>5.7</td>
<td>64</td>
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<td>Prince William County</td>
<td>475,533</td>
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<td>18</td>
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<td>19</td>
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<tr>
<td>PRINCE WILLIAM DISTRICT</td>
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<td>3.7</td>
<td>104</td>
<td>4.1</td>
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<tr>
<td>VIRGINIA</td>
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<td>169</td>
<td>2.0</td>
<td>161</td>
<td>1.9</td>
</tr>
</tbody>
</table>

[https://www.vdh.virginia.gov/tuberculosis/data-reports/]
3. Serial screening and testing for HCP without LTBI

However, consider:
- High risk occupational groups
- Settings with documented transmission
- Institutional or regulatory requirements
- Number active TB cases seen
- Delays in airborne isolation
- Environmental controls

No annual risk assessment either!
Annual education

All health care personnel should receive TB education every year.

Education template:
4. Evaluation and treatment of HCP with positive test results

- Risk assessment
- Symptom screen
- LTBI education
- Offer and encourage LTBI treatment

Must be conducted annually for HCP with untreated LTBI
TB screening/testing in other settings

- Visit our Screening & Testing webpage for resources
- Guidance for specific settings:
  - Corrections
  - Unhoused
  - Elderly Persons
    - High risk groups
    - Long-term care
VDH TB Website

VDH VIRGINIA DEPARTMENT OF HEALTH
To protect the health and promote the well-being of all people in Virginia

TUBERCULOSIS

Report Latent TB Infection (LTBI)

Local Health Districts - Report New Confirmed/Presumptive Active TB Cases

Local Health Districts - Report Initial 502 Information for New Contact Investigations

The mission of the Tuberculosis (TB) Program is to control, prevent, and eventually eliminate TB from the Commonwealth of Virginia. The program aims to detect every case of TB in Virginia, assure that every case is adequately and completely treated, and prevent transmission of TB in communities.

vdh.virginia.gov/tuberculosis
Questions?

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804-347-5712

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https://t.e2ma.net/click/ct3tvf/4mdrg1/4i23r5

#31 TB or Not TB, That Is the Infection Prevention Question