Guidelines for the Treatment of Latent Tuberculosis Infection (LTBI): Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Thursday, February 11th, 2021
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VDH TB Program

Polling Questions

Visit: www.ttpoll.com

Session ID:
WEBINAR GOALS

• Discuss why LTBI is an important issue in TB elimination
• Discuss the LTBI screening/testing/treatment process
• Describe currently recommended LTBI treatment regimens
• Identify what is new/different about recommendations
• Discuss benefits of implementation of recommendations
• Provide resources to help operationalize recommendations

VIRGINIA! Where in our lovely state are you located? *

* Please type in your location by state if not viewing from Virginia
What type of work organization are you linked to?

A-Public Health Departments and TB Programs
B-Community Health Clinics- includes Free/Charity, Rural Health
C-Hospital
D-Private Medical Practice
E-Long-Term Care
F-Correctional Facility-
G-Homeless Shelter
H-Other (enter in chat box)
BREAKING THE CYCLE OF LTBI PROGRESSION TO TB

- Ultimate goal is to interrupt transmission of active TB.
- Adherence to treatment of active TB interrupts direct transmission.
- Treating LTBI prevents TB by indirectly interrupting transmission.
- TB is thus not only treatable and curable, but also preventable.

PREVENTION OF ACTIVE TB VIA LTBI TREATMENT MAKES SENSE

<table>
<thead>
<tr>
<th>Individual</th>
<th>Organization</th>
<th>Society</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wellness</td>
<td>Investigations</td>
<td>Secondary transmission</td>
</tr>
<tr>
<td>Morale</td>
<td>Resources</td>
<td>Loss of work years</td>
</tr>
<tr>
<td>Productivity</td>
<td>Liability</td>
<td>Chronic morbidity</td>
</tr>
<tr>
<td>Lung health</td>
<td></td>
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</tbody>
</table>

- $19,000 TO TREAT TB DISEASE
- $600 TO TREAT LATENT TB INFECTION
- Treating latent TB infection is less costly than treating disease.
BURDEN OF LTBI IN THE UNITED STATES

Latent Tuberculosis Infection

Affects up to 13 MILLION people in the US.

Without treatment, 5 to 10% of infected persons will develop TB. Among those, 5 to 10% will develop TB within first 2 years of infection case.

LATENT TUBERCULOSIS (TB) BY-THE-NUMBERS


TB IN VIRGINIA (VA), 2010-2019

TB Cases, VA, 2010-2019

Year

Number of Cases


268 221 234 179 198 212 203 204 205 192

TB Case Distribution by Region, VA, 2010-2019


Central Eastern Northern Northwest Southwest
LTBI BURDEN IN VIRGINIA BY HEALTH PLANNING REGION

<table>
<thead>
<tr>
<th>Region</th>
<th>2019</th>
<th>2020</th>
<th>YTD 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>612</td>
<td>526</td>
<td>36</td>
</tr>
<tr>
<td>Eastern</td>
<td>829</td>
<td>630</td>
<td>22</td>
</tr>
<tr>
<td>Northern</td>
<td>4190</td>
<td>3858</td>
<td>273</td>
</tr>
<tr>
<td>Northwest</td>
<td>501</td>
<td>459</td>
<td>28</td>
</tr>
<tr>
<td>Southwest</td>
<td>551</td>
<td>360</td>
<td>13</td>
</tr>
<tr>
<td>Grand Total</td>
<td>6665</td>
<td>5568</td>
<td>411</td>
</tr>
</tbody>
</table>

Data is preliminary and subject to change

https://www.vdh.virginia.gov/content/uploads/sites/13/2016/03/Maps05-1.pdf

REACHING THE US GOAL OF TB ELIMINATION

- Modeling studies suggest TB elimination goal possible with LTBI testing/treatment increase strategy
- Finding/treating those at high risk for LTBI a priority as rate of active TB disease decreases
- Persons at high risk for LTBI fall into 2 categories:
  - Those who have been recently infected
  - Those with clinical conditions that increase risk of progressing from LTBI to TB disease
- Clinicians, health care agencies, & community organizations serving at-risk populations, critical to TB elimination goal
LTBI: SCREENING...TESTING....TREATMENT

Process of finding/treating those at high risk for LTBI entails:

- Conducting a risk assessment
  - Symptom review
  - LTBI risk
  - Risk for progression to TB if infected

- TB testing
  - IGRA or TST
  - Clinical evaluation to exclude TB disease if test results positive

- LTBI treatment initiation

What is the purpose of a TB risk assessment?
GROUPS AT RISK FOR LTBI OR FOR PROGRESSION TO TB ONCE INFECTED

True or False: “Not all individuals who complete a TB screening will need a TB test”

A. False

✓ B. True
In the past year, what treatment regimen did you often/most prescribe/favor for clients diagnosed with LTBI?

A. Daily INH (9 months)
B. Twice weekly INH (9 months by DOT)
C. Daily INH (6 months)
D. Twice weekly INH (6 months by DOT)
E. Rifampin (4 months)
F. INH-RPT 12 weekly dose (3 months)
G. INH-RIF (3 months)
THE NTCA/CDC 2020 UPDATED LTBI TREATMENT GUIDELINES:

- Systematic literature review by a CDC-NTCA committee
- Recommend the most effective & least toxic LTBI treatment regimens
- Recommend shorter treatment regimens that favor treatment completion
- Present the recommended treatment regimens in order of preference
- Recommend treatment regimens comprising
  - three preferred rifamycin-based regimens and
  - two alternative monotherapy regimens with daily isoniazid
- Encourage healthcare providers to prescribe these preferred shorter & more convenient regimens, when possible

EVIDENCE-BASED REVIEW: ‘GRADE’ CRITERIA APPLICATION
ELEMENTS OF 2020 UPDATED LTBI TREATMENT RECOMMENDATIONS
IN ORDER OF PREFERENCE

TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

<table>
<thead>
<tr>
<th>Priority rank</th>
<th>Regimen</th>
<th>Recommendation</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>3 mos isoniazid plus rifampin given once weekly</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Preferred</td>
<td>4 mos rifampin given daily</td>
<td>Strong</td>
<td>Moderate [HIV negative]</td>
</tr>
<tr>
<td>Preferred</td>
<td>3 mos isoniazid plus rifampin given daily</td>
<td>Conditional</td>
<td>Very low [HIV negative]</td>
</tr>
<tr>
<td>Alternative</td>
<td>6 mos isoniazid given daily</td>
<td>Strong</td>
<td>Moderate [HIV negative]</td>
</tr>
<tr>
<td>Alternative</td>
<td>9 mos isoniazid given daily</td>
<td>Conditional</td>
<td>Moderate [HIV positive]</td>
</tr>
</tbody>
</table>

Abbreviation: HIV = human immunodeficiency virus.

*Preferred: excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; alternative: excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

**No evidence reported in HIV positive persons.

*Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerance or drug-drug interactions).

THE 2020 UPDATED LTBI TREATMENT REGIMENS AT A GLANCE

Treatment regimens for latent TB infection (LTBI) use isoniazid (INH), rifampin (RFP), or rifampin (RIF). CDC and the National Tuberculosis Controllers Association preferentially recommend short-course, rifamycin-based: 6- or 4-month latent TB infection treatment regimens over 9- or 6-month isoniazid monotherapy.

Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coinfecting medical conditions (e.g., HIV+), and potential for drug–drug interactions.

https://www.cdc.gov/mmwr/volumes/68/wr/mm68013a1.htm#tuberculosis

NOTE: It is imperative to rule out active TB disease in all persons prior to initiating treatment for LTBI.
**PREFERRED RIFAMYCIN-BASED REGIMENS***

- Three preferred rifamycin-based regimens in preference order are:
  - 3 months of once-weekly isoniazid plus rifapentine (3HP)
  - 4 months of daily rifampin (4R)
  - 3 months of daily isoniazid plus rifampin (3HR)

- Preference based on effectiveness, safety, and high treatment completion rates.

- Should not be used for patients for whom rifamycins contraindicated
  - (including those taking medications with significant drug-drug interactions with rifamycin).

(*A rifamycin-based regimen includes either rifampin or rifapentine)
PREFERRED REGIMEN 2: 4R

- 4-month regimen of rifampin (RIF), given daily is the 2nd preferred regimen
- Should be completed within 6 months
- Recommended for HIV-negative adults and children of all ages
- Especially recommended for people who cannot tolerate INH or who have been exposed to INH-resistant TB
- Should not be used to treat HIV-infected people taking some combinations of antiretroviral therapy
- When rifampin (RIF) cannot be used, sometimes another drug, rifabutin (RBT), may be substituted

PREFERRED REGIMEN 3: 3HR

- 3-month regimen of INH and RIF given daily is the 3rd preferred regimen
- Recommended short-course for adults and children of all ages
- Recommended for HIV-negative and also for HIV-positive patients as drug interactions allow.
**ALTERNATIVE ISONIAZID MONOTHERAPY REGIMENS**

- Two alternative isoniazid monotherapy treatment regimens are the 4th preferred regimen

- Regimens of 6 or 9 months daily isoniazid with 6 months considered first

- Are as efficacious as rifamycin-based shorter-course regimens

- Higher toxicity risk

- Lower treatment completion rates

- Effectiveness decreased by higher toxicity risk/lower treatment completion rates.

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**ALTERNATIVE ISONIAZID MONOTHERAPY REGIMENS**

- Alternative regimens of 6 or 9 months daily INH when short-course treatment not an option

- 6H strongly recommended for HIV-negative adults & children of all ages

- 6H also a treatment option for HIV-positive adults & children of all ages

- 9H rated another option for HIV-negative/positive adults & children of all ages

- Daily self-administered treatments. May also be given twice weekly by DOT
<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Doses</th>
<th>Complete Within</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH-RPT (#1 preferred)</td>
<td>3 months</td>
<td>11-12</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Rifampin (#2 preferred)</td>
<td>4 months</td>
<td>120</td>
<td>6 months</td>
</tr>
<tr>
<td>INH-RIF (#3 preferred)</td>
<td>3 months</td>
<td>90</td>
<td>4 months</td>
</tr>
<tr>
<td>Daily INH (Alternative)</td>
<td>6 months</td>
<td>180</td>
<td>9 months</td>
</tr>
<tr>
<td>Twice weekly INH (Alternative)</td>
<td>6 months</td>
<td>52 DOT</td>
<td>9 months</td>
</tr>
<tr>
<td>Daily INH (Alternative)</td>
<td>9 months</td>
<td>270</td>
<td>12 months</td>
</tr>
<tr>
<td>Twice weekly INH (Alternative)</td>
<td>9 months</td>
<td>76 DOT</td>
<td>12 months</td>
</tr>
</tbody>
</table>

**MAKING A CASE FOR SHORTER-COURSE REGIMENS**

LTBI “Cascade of Care”

Alsdurf et al Lancet ID 2016
LTBI RESOURCES: HOT OFF THE PRESS......

NEW 2021 RESOURCE
TESTING AND TREATMENT OF LATENT TUBERCULOSIS INFECTION IN THE UNITED STATES:
CLINICAL RECOMMENDATIONS

• ‘Companion Document’ to 2020 LTBI treatment guidelines
• Developed by NTCA’s National Society of TB Clinicians (NSTC)
• A ‘living document’ with dynamic nature that resides on NTCA website - www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/#.YCAxtHdKIYU
• Practical guidance/clinical expertise to “put 2020 guidelines to work”
• Does not replace clinician clinical judgment
PRACTICAL GUIDANCE

- Determining when to test for LTBI, immunologic test to select/clinical interpretation of results
- Deciding whether to start client on LTBI treatment
- Prescribing correct drugs and dosing for treatment regimens
- Monitoring and managing LTBI Treatment
- Treatment options for specific populations, for example:
  - pregnant, breastfeeding and post partum clients
  - contacts to pan-susceptible and drug-resistant TB
  - LTBI clients with comorbidities that place them at higher risk for progression to TB

OTHER AVAILABLE LTBI RESOURCES**

Latent Tuberculosis Infection: A Guide for Primary Health Care Providers:  
www.cdc.gov/tb/publications/ltbi/default.htm

Latent TB Infection Treatment Regimens-Treatment Table  

Rutgers Global Tuberculosis Institute. Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider:  
2020 globaltb.njms.rutgers.edu/educationalmaterials/productfolder/ltbichildren

**Links to above resources, in addition to the February 14, 2020 guidelines and other VDH LTBI resources, can be found on the VDH TB Program webpage www.vdh.virginia.gov/tuberculosis/tb-infection-ltbi/
2020 UPDATED LTBI TREATMENT GUIDELINES SUMMARY

- Why act on recommendations?
  - Preferred regimens have excellent tolerability and efficacy, shorter treatment duration, and higher completion rates
  - Alternative regimens have excellent efficacy but longer treatment duration and lower completion rates
  - Assertion that shorter regimens have higher treatment completion rates is evidence-based
  - Both category regimens have similar efficacy
  - Shorter regimens therefore more effective due to higher completion rates

REFERENCES


Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection ATS/CDC Statement Committee on Latent Tuberculosis Infection Membership List, June 2000


Young, L. Tuberculosis Epidemiology: A Global, National and Virginia Update. March, 2020
Questions

A Q&A document will be provided to all attendees after the session.