Using the 12-Week INH-RPT Regimen for the Treatment of Latent TB infection

ITIH/LPH Webinar
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Outline

1. Background/introduction
2. 12-week INH-RPT regimen
3. Candidates for treatment
4. Monitoring pre- and during treatment
5. Obtaining medications from MDH TB program
6. Resources
Objectives: after completing this webinar, participants will be able to:

1. Identify appropriate candidates for the 12-week regimen for treating latent TB infection
2. Understand how to obtain this regimen from the MDH TB medications program
3. Locate and use resources designed to facilitate PHN supervision of someone taking this new regimen
**Someone with Latent TB Infection (LTBI)**

- Has a small amount of TB bacteria in their body that are alive, but inactive
- Cannot spread TB bacteria to others
- Does not feel sick, but may become sick if the bacteria become active in his/her body
- Usually has a positive TB skin test or TB blood test reaction
- Chest x-ray is typically normal
- Sputum smears and cultures are negative
- Should consider treatment for LTBI to prevent TB disease
- Does not require respiratory isolation
- Not a TB case. Not reportable in Minnesota.

Adapted from CDC Core Curriculum on Tuberculosis
LTBI in the United States

• Estimated >11 million persons
• Up to 10% will develop active TB disease if not treated, typically after 6-18 month latency period (or later)
Treatment for latent TB infection (LTBI)

- Essential to controlling and eliminating TB disease
- Reduces risk of LTBI progressing to active TB disease
- Use targeted testing to find persons at high risk for TB who would benefit from LTBI treatment
- Several treatment regimens available

Adapted from CDC Core Curriculum on Tuberculosis
LTBI Treatment Regimens*

- **Isoniazid**
  - 9 months
    - daily (preferred)
    - twice-weekly by DOT
  - 6 months
    - daily
    - twice-weekly by DOT

- **Rifampin (RIF)**
  - 4 months daily

- **INH and Rifapentine (INH-RPT)**
  - 3 months weekly by DOT

*Some regimens not appropriate in certain situations*
  - e.g., HIV-infected, children, pregnancy, suspected drug resistance, etc.
Almost 1/3 of high-priority LTBI patients in Minnesota do not complete therapy

- 65% of newly infected contacts in Minnesota in 2009 who started LTBI therapy completed treatment
  - United States: 67%

- 72% of TB Class B immigrants and refugees who started LTBI treatment completed treatment

- 72% of refugees who arrived in Minnesota in 2009 and who started LTBI therapy completed treatment
CDC recommendations based on:

1. 3 randomized clinical trials
   1. 2 large; 1 small
   2. Limited by unblinded design
   3. Completion of therapy higher for INH-RPT
   4. INH-RPT generally well-tolerated
2. CDC-convened panel of 23 experts April 2011
3. Experience with other LTBI regimens
INH-RPT: Pros and Cons

- **Advantages**
  - Fewer doses
  - Shorter treatment time
  - Higher completion of therapy rates
  - Was well tolerated in clinical trials

- **Disadvantages**
  - Not appropriate for all patients
  - Higher cost
  - DOT required
  - Large # of pills (up to 10)
INH-RPT is recommended for patients age ≥12 years with:

- Recent exposure to infectious TB
- Conversion from negative to positive TST or IGRA within previous 2 years
- Radiographic findings of inactive, “healed” pulmonary TB
- HIV/AIDS and not taking antiretroviral medications
- Medical or social circumstances that make adherence and completion of longer regimens unlikely
  - e.g., homeless, incarcerated, people who have failed to complete LTBI treatment previously, transplant list
Other immunosuppressive conditions

- Patients with other immune system disorders (e.g., diabetes) or taking certain drugs (TNF-alpha inhibitors, high-dose prednisone, etc.) were not included in the studies.
- MDH will supply INH-RPT on a case-by-case basis, at provider request.
INH-RPT not recommended for

- Children age <2 years
- Patients currently receiving antiretroviral treatment for HIV/AIDS
- Pregnant women or women expecting to become pregnant during treatment
- Persons with presumed INH or rifampin-resistant LTBI
Children aged 2-11 years

- Preferred regimen is 9 months of daily INH
- INH-RPT can be considered on a case-by-case basis when both
  - (1) the circumstances make the completion of 9 months of daily INH unlikely --AND--
  - (2) the likelihood or the risk of TB is great (e.g., recent *M. tuberculosis* infection in a preschool-aged child)
Rifamycins

Class of antibiotics most often used to treat mycobacterial infections

- Tuberculosis
- Hansen’s Disease (leprosy)
- *Mycobacterium avium complex* disease

**Most common:**

- Rifampin (RIF)
- Rifabutin
- Rifapentine (RPT)

- Cross-resistance is common
Rifapentine (PRIFTIN®)

- FDA-approved for treating TB disease
- “Off-label” use for LTBI
- Long plasma half-life
- 150 mg tablets
- Maximum dose is 900 mg = 6 tablets
- Packaged in blister packs
- Can cause orange-colored urine and tears
INH-RPT dosing (once weekly)

Isoniazid (INH)
- 15 mg/kg. Round up to the nearest 50 or 100 mg; maximum dose of 900 mg
- 100 mg and 300 mg tablets that can be split in half

Rifapentine (RPT)
- Maximum 900 mg
- 150 mg coated tablets
- Do not split

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<th>Weight (kg)</th>
<th>Recommended RPT dose</th>
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<tr>
<td>10 - 14</td>
<td>300 mg</td>
</tr>
<tr>
<td>14.1-25</td>
<td>450 mg</td>
</tr>
<tr>
<td>25.1 - 32</td>
<td>600 mg</td>
</tr>
<tr>
<td>32.1 – 49.9</td>
<td>750 mg</td>
</tr>
<tr>
<td>≥ 50</td>
<td>900 mg</td>
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</tbody>
</table>
INH-RPT Dosing, cont’d.

- Maximum dose = 9 tablets (3 INH + 6 RPT)

- Manufacturer is developing new formulations
  - larger dosage per tablets
  - fixed-dose INH-RPT combinations
INH-RPT dosing, cont’d.

• Ideally, doses should be spaced 7 days apart
• At a minimum, 72 hours must elapse between doses
• The minimum amount of time required is 12 weeks and the maximum is 16 weeks
• INH-RPT cannot be administered in less than 12 weeks
Pyridoxine (vitamin B6) supplementation

- Purpose: to prevent peripheral neuropathy as potential side effect of INH
- Not addressed in CDC recommendations
- Heartland National TB Center recommends using same criteria as for 9 months of INH
  - Diabetes, renal failure, alcoholism, malnutrition, HIV infection, seizure disorder
  - Weekly B6 dosing is OK
DOT for INH-RPT LTBI regimen

- MDH and Heartland National TB Center recommend DOT by local public health
  - Potential exceptions: corrections, college health services
- Self-administered regimen currently being studied
Local Public Health role

• LPH agencies should determine the feasibility of providing INH-RPT

• Factors to consider:
  ▫ Patient’s risk of developing active TB
  ▫ Available local resources for providing DOT
  ▫ The capacity for monthly patient monitoring
  ▫ Patient’s likelihood of successfully completing treatment
  ▫ Patient and provider preference
Pre-treatment evaluation

- Rule out active TB disease
- History of treatment for LTBI or disease
- Contraindications to treatment
- Current and previous drug therapy history, including adverse reactions
- Rule out pregnancy
- HIV testing recommended (opt-out)
Potential drug-drug interactions

- INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse)
- RPT has high risk for drug-drug interactions
  - decreases blood levels of many drugs
  - hormonal contraceptives,
  - warfarin,
  - sulfonylureas (diabetes),
  - Methadone
  - Etc,
  - Contraindicated in HIV-infected individuals being treated with protease inhibitors (PIs) and most nonnucleoside reverse transcriptase inhibitors
Potential adverse drug reactions

- Liver toxicity (INH)
- Hypersensitivity (RPT)
  - Hypotension
    - Mild: treat with rest and oral fluids
    - Extreme: hold medications and evaluate
- Thrombocytopenia
Pregnancy and Rifapentine

• RPT has not been adequately studied in pregnancy
• INH-RPT not recommended for pregnant women or women who plan to become pregnant during treatment
• If using hormonal contraceptives, add barrier method
• If pregnancy occurs, discontinue INH-RPT
Pre-treatment education

• Commit to 12 weeks of weekly DOT
• Agree to take up to 9-10 tablets each time
• Avoid pregnancy
• Schedule monthly physical examinations
• If these cannot reasonably be assured, one of the other LTBI treatment regimens should be used
Other factors to consider

1. Does patient fully understand the regimen?
2. RPT supply adequate for entire 12 weeks?
3. Is patient planning to move? If so, check with new jurisdiction to ensure that INH-RPT can be provided there
4. Any trips planned?
Laboratory testing: initial

- Baseline laboratory monitoring during treatment of LTBI is not routinely recommended by CDC
- Should be provided for certain high-risk patients
  - HIV+
  - At risk for liver disorders
  - Immediate post partum (3 months)
  - Regular alcohol usage
  - (Age over 50 years)
  - Provider judgment
Laboratory testing: follow-up

- Follow-up laboratory monitoring during treatment of LTBI not routinely recommended
- Should be provided for certain high-risk patients
  - Abnormal baseline results
  - HIV+
  - Liver disorders
  - Immediate post partum (3 months)
  - Regular alcohol usage
Monitoring: Weekly DOT Visits

- Assess for evidence of hepatitis or other adverse effects, including drug hypersensitivity reactions
- Active TB symptoms?
- Instruct patient to seek medical attention immediately if:
  - fever
  - jaundice
  - dizziness
  - rash
  - aches
  - >1 day of nausea, vomiting, weakness, abdominal pain, or loss of appetite.
- Withhold medication while cause of symptoms being evaluated
Monthly physical examination

- Assess for liver toxicity
  - jaundice, liver tenderness, rash
- Other side effects
- Signs of active TB disease
Reporting severe adverse events

- With previous LTBI regimens (e.g., INH, rifampin-pyrazinamide), fatal liver injuries came to attention only after the regimens were widely adopted.
- Adverse events leading to hospitalization or death associated with the use of any LTBI regimen should be reported to
  - MDH (651-201-5414) for inclusion in CDC’s adverse events surveillance system, -AND-
MDH TB Medications Program

- LTBI or active TB disease
- Free of charge for residents of Minnesota
- CDC/ATS treatment guidelines
- Call MDH to request (651) 201-5506
- Sent monthly to health care worker to dispense and monitor
Obtaining INH-RPT from MDH

- Meet eligibility criteria **AND** specific plan to provide monthly physical examinations and DOT
- Submit the Request for Medication to Treat Latent TB Infection (LTBI) form
- Lenette will supply a “INH-RPT Checklist” form for you to complete and return to MDH
  - Which criteria apply?
  - DOT provider name and agency
  - Monthly physical exam provider
  - Patient teaching
- Shipments will be monthly x3
- Notify MDH ASAP if treatment stopped early!
Revised/new MDH materials

- Web site
- MDH written recommendations for INH-RPT (new)
- Eligibility Criteria for the Use of the 12-week INH-RPT Regimen (new)
- Evaluation and Monitoring during Treatment of LTBI
- LTBI Dosing: INH-RPT (new)
- Recommended Regimens for Treatment of LTBI
- Request for Medication to Treat Latent TB Infection (LTBI)
- Treatment of LTBI Monitoring Flow Sheet
- Completion of Therapy for Latent Tuberculosis Infection (LTBI) “Gaps rules”
Evaluation

• MDH plans to evaluate the use of the INT-RPT regimen
• Contact providers and/or LPH
  ▫ Completion of therapy
  ▫ Obstacles
  ▫ Benefits
  ▫ Cost
CDC resources

• New Treatment Regimen for Latent Tuberculosis Infection
  http://www.cdc.gov/tb/topic/treatment/12dose_video.htm

• Web Feature - New, Simpler Way to Treat Latent TB Infection
  http://www.cdc.gov/Features/TuberculosisTreatment/
  ▫ Spanish Version - (Español):
  ▫ http://www.cdc.gov/spanish/especialesCDC/TratamientoTB/

• Treatment Options for Latent TB Infection (Fact Sheet)

• Treatment for Latent TB Infection (webpage)
  http://www.cdc.gov/tb/topic/treatment/ltbi.htm
Thank you to:

- Medical and nursing staff at
  - Hennepin County Public Health TB Clinic
  - Olmsted County TB Clinic
  - St. Paul Ramsey County Public Health TB Program
Think TB!

Questions about TB?
Call the Minnesota Department of Health at
651-201-5614
www.state.mn.us/tb