OBJECTIVE: To guide appropriate, evidence-based screening, diagnosis and treatment of pediatric latent TB infection (LTBI) in outpatient clinic settings

Specific Objectives:
1. To provide criteria for screening, diagnosing and treating pediatric LTBI
2. Potential measurable outcomes after initiation of guideline:
   a. Patients who meet criteria appropriately screened with testing for LTBI
   b. Patients diagnosed with LTBI who receive INH treatment
   c. Documentation of INH treatment completion in chart

SUMMARY:
BRIEF summary of recommendations
1. At each annual well child exam, screen verbally for latent TB risk factors with recommended screening questions:

<table>
<thead>
<tr>
<th>Validated Questions for Determining Risk of LTBI in Children in the United States</th>
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<tbody>
<tr>
<td>1. Has a family member or contact had tuberculosis disease?</td>
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<td>2. Has a family member had a positive tuberculin skin test result?</td>
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<td>3. Was your child born in a high-risk country (countries other than the United States, Canada, Australia, New Zealand, or Western European countries)?</td>
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<td>4. Has your child traveled (had contact with resident populations) to a high-risk country for more than 1 week?</td>
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<td>5. Additional question recommended by SCH Infectious Diseases Team: Have there been any household visitors from high-risk countries?</td>
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2. Screening tests should be done based on risk factors for exposure and risk of progression from latent to active TB.
3. Screening tests differ by age group, with tuberculin skin test (TST or PPD) preferred under age 5 years and quantiferon gold preferred for ages 5 and above. Use both tests when there are indeterminate results or concern for false positives or negatives to help establish diagnosis.
4. If positive test results, establish diagnosis of latent TB infection by ruling out active disease through chest x-ray, history and exam.
5. Provide treatment with isoniazid (INH) for 9 months.
Pediatric Latent TB Diagnosis and Treatment

1. Inclusion Criteria
   a. All pediatric patients should receive verbal screening annually for TB risk factors at well child checks, and those who have risk factors should have TB testing.

2. Exclusion Criteria
   a. This guideline does not apply to those diagnosed with active TB or those with a history of a prior positive TB test who have already received treatment.

3. Administer TB screening tests for pediatric populations that are high risk including:
   a. Close contacts of persons known or suspected to have active TB
   b. Visiting grandparents, foreign-born nannies or parents who immigrated (if not tested and negative)
   c. Individuals born in or who visit (>1week) countries with higher incidence of active TB (Asia, Middle East, Africa, Latin America, countries of the former Soviet Union)
   d. Living in settings with higher TB prevalence (i.e. prison, homeless or shelters, with IV-drug users)
   e. Local populations with increased incidence of TB (medically underserved, low-income or persons abusing drugs/ alcohol)
   f. Give special consideration for children at increased risk of progression from LTBI to active disease
      i. Infants and children < 5 years of age with recent TB contact
      ii. HIV infection
      iii. Immunosuppressive therapy
         1) TNF-alpha antagonists
         2) High-dose steroids (≥2mg/kg (or ≥20mg)/day prednisone x 14+ days)
         3) organ transplant recipients
   iv. TB infection within the past 2 years
   v. History of inadequately or untreated active TB (evidence of fibrotic changes on CXR)
   vi. Chronic renal failure, poorly controlled diabetes mellitus, leukemia, lymphoma
   vii. Malnutrition (weight <90% IDW)
   viii. Primary Immunodeficiency

4. Screening tests to use for diagnosis of LTBI based on age
   a. 3 months – 2 years old
      i. Tuberculin skin test (TST=PPD)
   b. 2-5 years old
      i. TST preferred, Interferon Gold release assay (IGRA*) acceptable only if TST negative and risk for TB exposure is high.
   c. Children > 5 years
Pediatric Latent TB Diagnosis and Treatment

i. IGRA recommended
d. Children BCG-vaccinated or < 5 years who are unlikely to return for TST reading
   i. IGRA preferred, TST acceptable
e. Special populations
   i. Patients with HIV-use TST
   ii. Patients who have had a prior positive TST or Quantiferon, regardless of LTBI treatment, should not have repeat TB test (+TST and Quantiferon will remain positive and are no longer diagnostic)
f. Special circumstances - use both TST and IGRA
   i. When the initial and repeat IGRA results are indeterminate
   ii. The initial test (TST or IGRA) is negative and
       a) There exists clinical suspicion for TB disease
       b) Risk of infection with poor outcome is higher
   iii. The initial TST is positive and:
       a) >5 years of age and history of BCG vaccination
       b) Need additional evidence to increase compliance
       c) Nontuberculous mycobacterial infection is suspected

5. Timing of screening
   a. Immediately if any known exposure to TB
      i. Recognize that conversion to positive PPD may take 2-10 weeks, so repeat testing would be indicated for some situations.
      ii. Note: Only place TST (PPD) when it can be evaluated in 48-72 hours (i.e., do not place on Thursday unless Saturday/Sunday reading is available)
   b. 10 weeks after travel to an endemic country, but ok to wait until annual physical
   c. Wait 1 month after brief pulse steroids for asthma and 2 months after higher dose (15mg/day) or more chronic steroids that required a taper
   d. Wait 4-6 weeks after live virus vaccines (MMR, Varicella, FluMist) if not administered concurrently

6. Diagnosis of a positive result
   a. TST Results as Positive (*regardless of BCG status)
      Note: refer to CDC guidelines for help with reading PPD
      http://www.cdc.gov/tb/publications/factsheets/testing/skintesting.htm
      i. Induration 5 mm or greater
         a) Children in close contact with TB or clinically suspicious for having TB
         b) Immunosuppressed children (HIV or steroids/chemo/biologics)
      ii. Induration 10 mm or greater
         a) Children at increased risk of disseminated TB:
         b) Children < 4 years
         c) Children with Hodgkins, lymphoma, diabetes, renal failure, malnutrition
         d) Children with likelihood of increased exposure to tuberculosis disease:
            o Children born in high-prevalence regions of the world
            o Children who travel to high-prevalence regions of the world
Pediatric Latent TB Diagnosis and Treatment

- Children frequently exposed to adults with HIV, who are homeless, incarcerated or institutionalized, use drugs, or reside in nursing homes
  iii. **Induration 15 mm or greater**
    a) Children age 4 years or older without any risk factors

7. Next steps based on results
   a. Negative -> if rule out false negative -> done
   b. Positive -> Must rule out active disease
      i. Get chest x-ray (CXR)
      ii. **Review TB symptoms**, including: cough, fever, night sweats, weight loss, and hemoptysis
      iii. **Inquire about household contacts** who may require TB testing or who have active TB disease
      iv. **Physical exam** – look for signs of pulmonary or extra-pulmonary TB infection on physical exam
      v. **If active disease is diagnosed or highly suspected**, immediately consult pediatric infectious disease specialists and public health officials.
   c. If indeterminate -> obtain whichever test was not originally done: TST or IGRA. Interpret test results based on the following guidelines if there is no suspicion for active TB:

<table>
<thead>
<tr>
<th>TST</th>
<th>IGRA</th>
<th>Patients with no clinical suspicion for active tuberculosis disease</th>
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<tr>
<td>(+)</td>
<td>(-)</td>
<td>If BCG vaccinated and ≥5 years of age, may discount TST &lt;15 mm if patient has low risk for latent TB infection or poor outcome. Otherwise, treat for LTBI.</td>
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<tr>
<td>(-)</td>
<td>(+)</td>
<td>Treat for LTBI. Consider ID consult.</td>
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8. Treatment
   a. INH x 9 months (scored tabs 100mg, 300mg, syrup 10mg/mL)
      i. Dose for children <15 yo and/or <40 kg is 10-20mg/kg/day (max 300mg/day)
      ii. Dose for children ≥15 yo or >40 kg is 5 mg/kg/day (max 300mg/day)
      iii. Routine determination of serum transaminase values is not indicated, unless history of liver disease or risk for liver disease (alcohol abuse, IV drug use, viral hepatitis (B or C), or cirrhosis, or <3 months post-partum)
         1) Counsel to avoid Tylenol and alcohol
      iv. Side effects of INH
         1) diarrhea and gastric irritation caused by vehicle in the syrup
         2) Neuropathy (peripheral neuritis or seizures) rare in children
v. Pyridoxine (vitamin B6) supplement of 25-50mg/day recommended for a few groups:
   o exclusively breastfed infants, children with nutritional deficiencies or on meat- and milk-deficient diets
   o symptomatic HIV-infected children
   o pregnant adolescents and women

b. For cases where 9 months INH is not possible, see CDC website for alternative regimens including a 12 week combination regimen of INH and rifapentine with directly observed therapy (DOT) for children > 2 yo. Requires monthly clinical monitoring for side effects.

9. Follow-up: use active case management, especially in the first 3 months of therapy, to establish INH adherence and screen for side effects. An initial in-person visit (with a nurse or medical provider) should be considered at 1 month, with option to follow care by telephone calls for subsequent months.

10. Differential Diagnoses to consider
   a. Must rule out active TB infection

11. Pitfalls/Things to be aware of
   a. False negatives
      i. Window period of 2-10 weeks after exposure before tests are positive.
      ii. Following pulse steroids for asthma (see above)
      iii. After live virus vaccines (MMR, Varicella, FluMist) (see above)
   b. System barriers for families to complete INH regimen
      i. work closely with family to support completion of therapy
      ii. ensure appropriate pharmacy selected
      iii. use active case management with monthly calls and monitoring adherence of picking up medication