

TB Infection in the Pediatric Population

- Testing and Treatment

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Disclosures

- No financial conflicts or disclosures
- Heavily utilizes AAP and CDC approved guidance
- New TB infections in children are a sentinel health event

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Outline

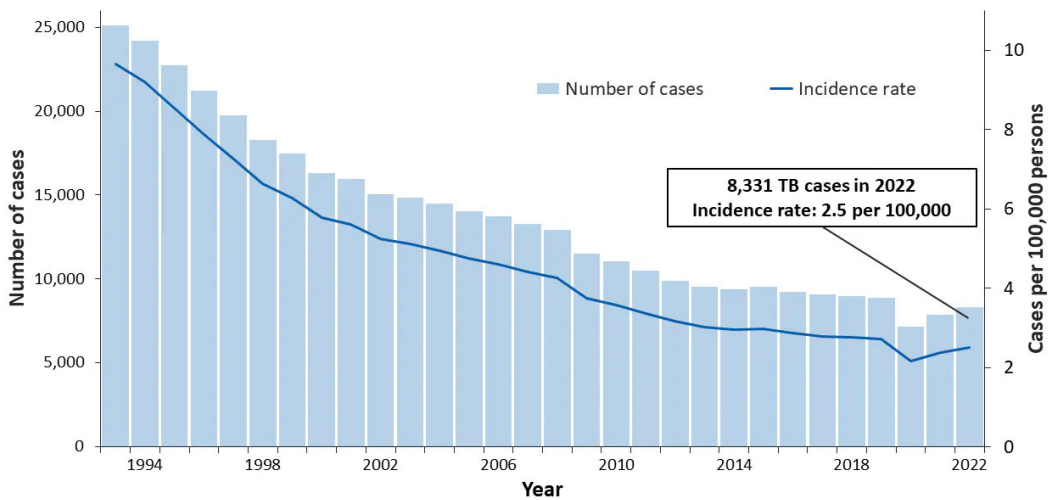
- Epidemiology
- Differences and Similarities
- TB Exposure
 - Risk Assessment
 - Testing
 - Window Prophylaxis
- TB Infection
 - Education
 - Treatment

Definitions

- TB Exposure
 - Asymptomatic
 - TST/IGRA negative
 - CXR normal
- TB Infection
 - AKA LTBI
 - Asymptomatic
 - TST/IGRA positive
 - CXR normal or calcifications
- TB Disease
 - Symptomatic
 - TST/IGRA positive (*can be negative*)
 - CXR abnormal (*usually*)

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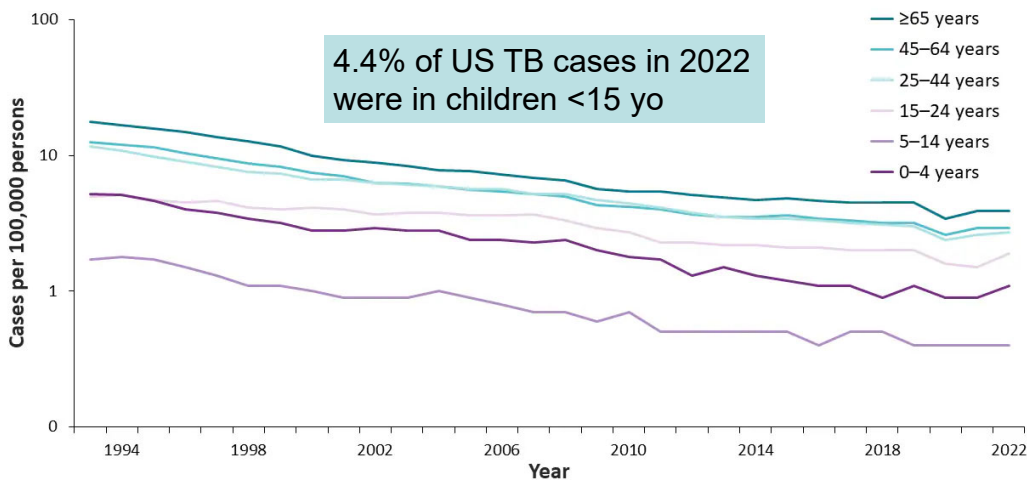
TB Cases and Incidence Rates, United States, 1993–2022



https://www.cdc.gov/tb/statistics/reports/2022/national_data.htm 7/2/2024

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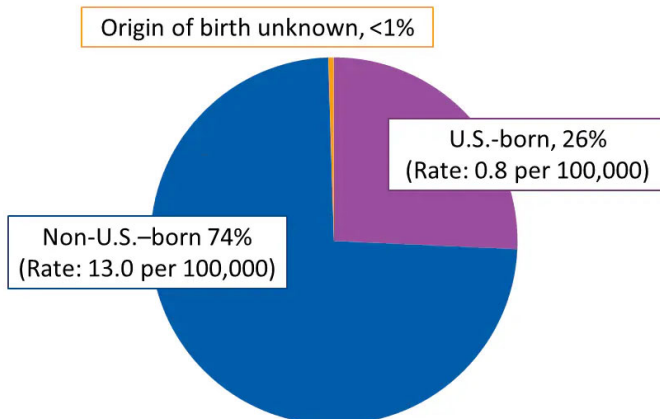
TB Incidence Rates by Age Group, United States, 1993–2022



<https://www.cdc.gov/tb/statistics/reports/2022/demographics.htm#Age> 7/2/2024

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TB Incidence Rates and Percentages by Origin of Birth,* United States, 2022 (N=8,331)

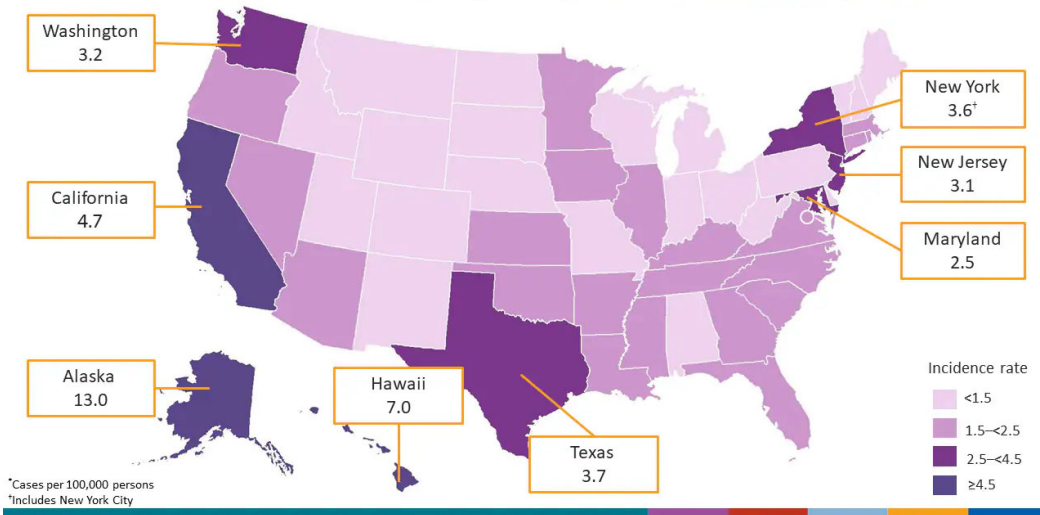


*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.-born.

<https://www.cdc.gov/tb/statistics/reports/2022/demographics.htm#Age> 7/2/2024

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TB Incidence Rates* by Reporting Area, United States, 2022



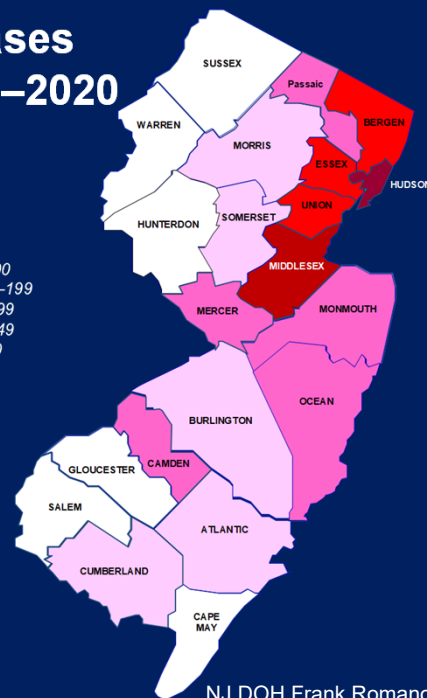
https://www.cdc.gov/tb/statistics/reports/2022/state_local_data.htm 7/2/2024

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Counted TB Cases New Jersey, 2016–2020

TB Incidence Cases by County
New Jersey, 2023 (N= 343)

| County | Cases | Percent | Cum. Percent | IR* |
|--------------|------------|----------------|----------------|-----|
| Middlesex | 67 | 19.53% | 19.53% | 7.8 |
| Hudson | 56 | 16.33% | 35.86% | 7.9 |
| Essex | 45 | 13.12% | 48.98% | 5.3 |
| Union | 29 | 8.45% | 57.43% | 5.1 |
| Bergen | 28 | 8.16% | 65.60% | 2.9 |
| Passaic | 24 | 7.00% | 72.59% | 4.7 |
| Somerset | 19 | 5.54% | 78.13% | 5.4 |
| Burlington | 15 | 4.37% | 82.51% | 3.2 |
| Mercer | 15 | 4.37% | 86.88% | 3.9 |
| Monmouth | <10 | N/A | N/A | N/A |
| Morris | <10 | N/A | N/A | N/A |
| Ocean | <10 | N/A | N/A | N/A |
| Camden | <10 | N/A | N/A | N/A |
| Atlantic | <10 | N/A | N/A | N/A |
| Gloucester | <10 | N/A | N/A | N/A |
| Cumberland | <10 | N/A | N/A | N/A |
| Hunterdon | <10 | N/A | N/A | N/A |
| Cape May | 0 | N/A | N/A | 0.0 |
| Salem | 0 | N/A | N/A | 0.0 |
| Sussex | 0 | N/A | N/A | 0.0 |
| Warren | 0 | N/A | N/A | 0.0 |
| TOTAL | 343 | 100.00% | 100.00% | |



*Incidence Rate (Cases per 100,000 population)
Data Source: US Census Bureau, Population estimates, July 1, 2023, (V2023)

<https://www.nj.gov/health/hivstdtb/documents/tb/tb-risk-assessment-data-2023.pdf> 7/2/2024

NJ DOH Frank Romano

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LTBI – CDC Estimates

- Up to 13 million people in the US with LTBI
- Reactivation of LTBI
 - Risk adjusted by co-morbidities
 - Future therapies
- LTBI → TB disease is responsible for approx. 80% of US TB cases
- Remember sentinel event
- Active TB risk
- Reactivation or Primary
- Children
 - 40 to 50% infants
 - 5 to 15% children
 - Risk highest in the 1 to 2 years after infection
- Adult data
 - 5 to 10% lifetime risk
 - 50% of the risk in the first 2 years

<https://www.cdc.gov/tb/hcp/clinical-overview/latent-tuberculosis-infection.html> 7/1/2024

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- 1) + Test (IGRA or TST)
- 2) No signs or symptoms of disease
- 3) - CXR

DIAGNOSING LTBI IN CHILDREN

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TESTING

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Diagnosis of TB Infection

- TST
 - Various criteria for “positive”
 - Limitations
 - Observer variability
 - Return for reading
 - Cross reacting antigens

- Interferon Gamma Release Assays (IGRA)
 - Lymphocytes stimulated by *M. tuberculosis* Ag
 - Does not recognize BCG
 - Limited data on accuracy in young children and immunosuppressed
 - Limited data <2yo
 - Gaining acceptance
 - Interpretation of “indeterminant”

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Table 3.75. Tuberculin Skin Test (TST) and IGRA Recommendations for Infants, Children, and Adolescents^a

Travel Question
>2 weeks?
Exposure?

Consider delaying
testing 8-10 weeks



- Children for whom immediate TST or IGRA is indicated^b:
- Contacts of people with confirmed or suspected tuberculosis (contact investigation)
 - Children with radiographic or clinical findings suggesting tuberculosis disease
 - Children immigrating from countries with endemic infection (eg, Asia, Middle East, Africa, Latin America, countries of the former Soviet Union), including international adoptees
 - Children with history of significant^c travel to countries with endemic infection who have substantial contact with the resident population^d

- Children who should have annual TST or IGRA:
- Children living with HIV infection

Children at increased risk of progression of TBI to TB disease: Children with other medical conditions, including diabetes mellitus, chronic renal failure, malnutrition, congenital or acquired immunodeficiencies, and children receiving tumor necrosis factor (TNF) antagonists, deserve special consideration. Underlying immune deficiencies associated with these conditions theoretically would enhance the possibility for progression to severe disease. Initial histories of potential exposure to tuberculosis should be included for all these patients. If these histories or local epidemiologic factors suggest a possibility of exposure, immediate and periodic TST or IGRA should be considered. **A TST or IGRA should be performed before initiation of immunosuppressive therapy, including prolonged systemic corticosteroid administration, organ transplantation, use of TNF-alpha antagonists or blockers, or other immunosuppressive therapy in any child requiring these treatments.**

AAP Red Book 2021-2024

Pediatric Tuberculosis (TB) Risk Assessment



Please select Yes or No for each of the following questions to assist your child's pediatrician:

| | | |
|---|--|--|
| Does your child have any symptoms of TB (cough, fever, night sweats, loss of appetite, weight loss, less playful or energetic, showing signs of being more tired than usual)? | <input type="radio"/> Yes | <input type="radio"/> No |
| Has your child spent time with anyone sick with TB? | <input type="radio"/> Yes | <input type="radio"/> No |
| In the last 12 months, has your child lived with or spent significant time with anyone with a long-lasting cough? | <input type="radio"/> Yes | <input type="radio"/> No |
| Has your child had a chest X-ray in the past year? | <input type="radio"/> Yes | <input type="radio"/> No |
| TB is more common in countries in Asia, the Middle East, Africa, Latin America, Eastern Europe and the former Soviet Union | | |
| Were you or your child born in a country that is in an area listed above? | <input type="radio"/> Yes | <input type="radio"/> No |
| In the past 2 years, have you or your child traveled to a country that is in an area listed above? If yes, did you or child spend most of the time with family and friends or other people in the community? | <input type="radio"/> Yes <input type="radio"/> Yes | <input type="radio"/> No <input type="radio"/> No |
| In the past 2 years, have you had visitors from outside of the U.S. visit your home for at least 14 days? If yes, please write which country they visited from: _____ | <input type="radio"/> Yes | <input type="radio"/> No |
| Does your child have HIV infection? | <input type="radio"/> Yes | <input type="radio"/> No |
| Does your child have diabetes? | <input type="radio"/> Yes | <input type="radio"/> No |
| Does your child have a serious kidney disease? | <input type="radio"/> Yes | <input type="radio"/> No |
| Has your child been diagnosed with a weakened immune system? If yes, is your child taking medication for this? | <input type="radio"/> Yes <input type="radio"/> Yes | <input type="radio"/> No <input type="radio"/> No |
| Is your child taking medication for nephrotic syndrome (a kidney disorder), rheumatoid arthritis, Crohn's disease, or similar conditions? | <input type="radio"/> Yes | <input type="radio"/> No |
| Is your child currently taking steroids, or have they ever taken steroids for 2 weeks or more? | <input type="radio"/> Yes | <input type="radio"/> No |
| Has your child had an organ transplant? | <input type="radio"/> Yes | <input type="radio"/> No |

<https://globaltb.njms.rutgers.edu/education/materials/productfolder/PEDSTool.php>

Table 3.74. Definitions of Positive Tuberculin Skin Test (TST) Results in Infants, Children, and Adolescents^{a,b}

- ★ **Induration 5 mm or greater**
 Children in close contact with known or suspected contagious people with tuberculosis (TB) disease
 Children suspected to have TB disease:
 - Findings on chest radiograph consistent with active or previous TB disease
 - Clinical evidence of TB disease^c
 Children receiving immunosuppressive therapy^d or with immunosuppressive conditions, including human immunodeficiency (HIV) infection
- ➔ **Induration 10 mm or greater**
 Children at increased risk of disseminated TB disease:
 - Children younger than 4 y
 - Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition (see Table 3.75)
 - Children born in high-prevalence regions of the world
 - Children with significant travel to high-prevalence regions of the world^e
 - Children frequently exposed to adults who are living with HIV, experiencing homelessness, or incarcerated, or to people who inject or use drugs or have alcohol use disorder
- ✘ **Induration 15 mm or greater**
 Children without any risk factors

AAP Red Book 2021-2024

**TST or IGRA
Which is really better?**

Sensitivity

- TST 80% (70-90)
- QFN TB 83% (75-92)
- T-SPOT 84% (63-100)

Specificity

- TST 85% (63-100)
- QFN TB 91% (78-100)
- T- SPOT 94% (87-100)

- IGRA indeterminate rate 3-6%
(Young age, helminth, immunosuppression)

Mandalakas, et al. IJTL 2011

LTBI EVALUATION AND TREATMENT

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Diagnosis of Latent Infection

- Positive tuberculin skin test (TST) or Interferon Gamma release assay (IGRA)
- Normal CXR or evidence of healed infections (calcified granuloma in lungs or calcification in lymph nodes)
- No signs or symptoms of TB disease

2 view CXR in <5 y/o
Read by pediatric radiologist



Thorough H&P

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Varied Manifestations of TB Disease

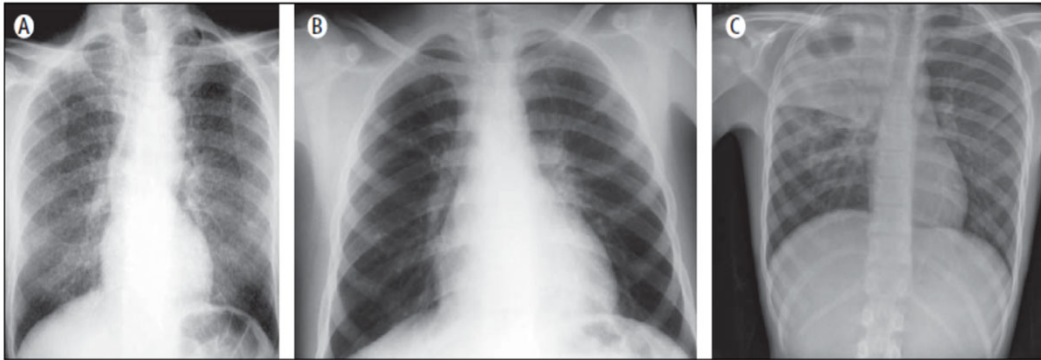
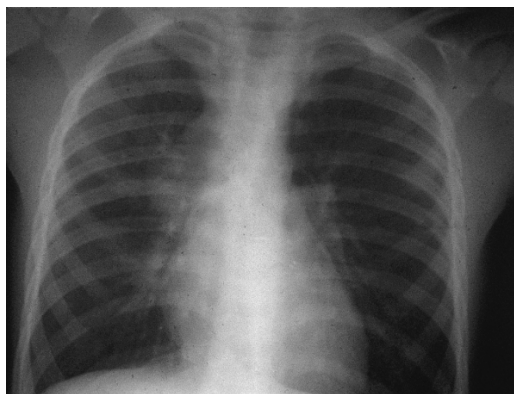


Figure 1: Radiological presentation of tuberculosis in childhood
(A) Miliary tuberculosis. (B) Hilar lymphadenopathy. (C) Cavitating lung disease (adult type).

Newton, et al. Lancet ID 2008

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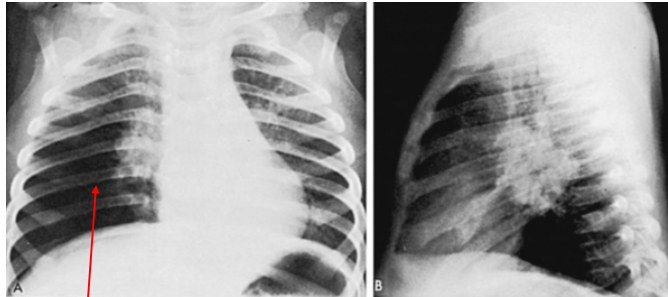
Primary Pulmonary Disease



Right-sided hilar lymphadenopathy with minor parenchymal infiltrate in a 3-year-old boy with primary pulmonary tuberculosis

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Adenopathy



hyperaeration

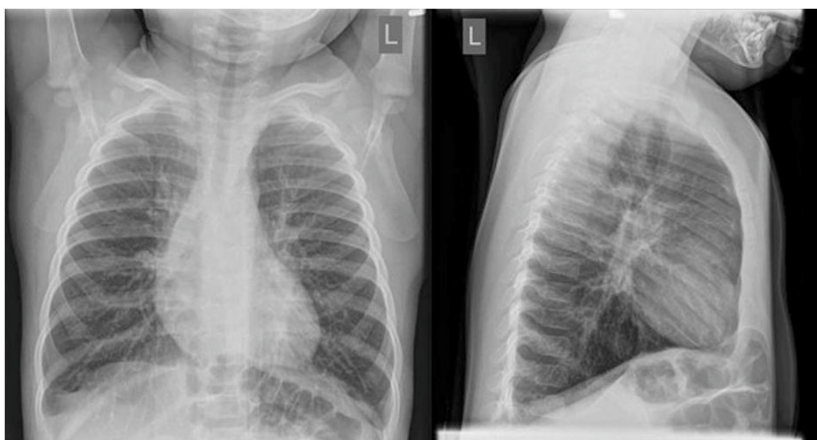
Note the degree of adenopathy on both projections

From Starke Chapter 107 in Textbook of Pediatric ID 2009

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Abnormal but not Suggestive of TB

- 2 years old
- Afebrile
- Wheezing
- Consider repeating



hyperinflation with flattened diaphragms, peribronchial thickening with subsegmental atelectasis

Friedman et al. BMJ 2021

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Symptom Screen

- Cough >3 weeks
- Hemoptysis
- Weight loss
- Fever, chills, night sweats
- Dyspnea
- Fatigue
- Chest pain

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Evaluation of Contacts of a Person with Infectious TB

Contacts at High Risk for Rapid Development of TB Disease

Sometimes LTBI treatment is given to people who have a negative TST or IGRA result. For example, some contacts at high risk for rapidly developing TB disease should start LTBI treatment even if they have a negative test and less than 8 to 10 weeks have passed since they were last exposed to TB. These contacts include

- Children who are younger than 5 years of age (some TB programs may have different age cutoff guidelines)
- People living with HIV

Some contacts may start taking LTBI treatment if they have a negative TST or IGRA result but less than 8 to 10 weeks have passed since they were last exposed to TB.

Window Prophylaxis

Once TB disease is ruled out, these contacts should start LTBI treatment to prevent them from rapidly developing TB disease. They also should be retested 8 to 10 weeks after they were last exposed to TB. If the contact has a positive TST or IGRA result, he or she should continue to take LTBI treatment. Contacts living with HIV may be given a full course of LTBI treatment even if their second TST or IGRA result is negative.

Rule Out TB Disease

1. Symptoms
2. PE
3. CXR

TB contacts living with HIV may be given a full course of LTBI treatment even if their second TST or IGRA result is negative.


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Usually not an Emergency

LTBI TREATMENT

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| COMMONLY USED PEDIATRIC TREATMENT REGIMENS ¹ (for those infected with presumed drug-susceptible <i>M.tb</i>); consult an expert for exposure to drug-resistant TB) | | | |
|--|---|---|--|
| REGIMEN | DOSAGE | | COMMENTS |
| 12 Weeks of Once-Weekly Isoniazid (INH) Plus Rifapentine Administration: DOT or SAT ² Completion Criteria: 12 doses within 16 wks. | 2-11 Years INH: 25 mg/kg; rounded up to the nearest 50 or 100 mg (max 900 mg) | ≥12 Years INH: 15 mg/kg rounded up to the nearest 50 or 100 mg (max 900 mg) | <ul style="list-style-type: none"> Preferred by most experts for treatment of LTBI in children ≥2 years of age Not indicated for: <ul style="list-style-type: none"> Children <2 years of age Children with <i>M.tb</i> infection that is presumed resistant to INH and/or RIF Children who had prior adverse events or hypersensitivity to INH, RIF, or rifapentine Pregnant adolescents Pill burden is substantial for young children and sometimes is not well tolerated Should take with food containing fat, if possible Rifapentine may not be readily available |
| | Rifapentine: 10-14.0 kg: 300 mg 14.1-25.0 kg: 450 mg 25.1-32.0 kg: 600 mg 32.1-49.9 kg: 750 mg ≥50.0 kg: 900 mg | | |
| 4 Months of Daily Rifampin (RIF) Administration: SAT ² Completion Criteria: 120 doses within 6 mos. | 15-20 mg/kg; max 600 mg | | <ul style="list-style-type: none"> Widely used in children and adolescents Continuous daily therapy is required Consider drug-drug interactions (see next column) |
| 6 or 9 Months of Daily INH³ Administration: SAT ² Completion Criteria: 6 mo. regimen: 180 doses within 9 mos. 9 mo. regimen: 270 doses within 12 mos. | 10-15 mg/kg; max 300 mg | | <ul style="list-style-type: none"> Many providers use the INH regimen only when a rifamycin-based regimen cannot be used; long duration can result in poor adherence and lower completion rates Although 9 mos. duration is recommended for children (including those with HIV or other immunosuppression), CDC and many experts accept 6 consecutive mos. of uninterrupted daily therapy as adequate |



For additional resources

RUTGERS
Global Tuberculosis Institute
NEW JERSEY MEDICAL SCHOOL

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Short Course Regimen: INH + Rifapentine 12 Dose Regimen

PROs

- INH + Rifapentine + B6 once a week x 12 weeks
- Adherence better

CONs

- Pill burden (10 pills in adult dose)
- DOT preferred
- Rifapentine information lacking for some groups

| MARCH 2017 | | | | | | | APRIL 2017 | | | | | | | MAY 2017 | | | | | | | |
|------------|----|----|----|----|----|----|------------|----|----|----|----|----|----|----------|----|----|----|----|----|----|---|
| S | M | T | W | T | F | S | S | M | T | W | T | F | S | S | M | T | W | T | F | S | |
| | | | | 1 | 2 | 3 | 4 | | | | | | 1 | | | | | | | | 1 |
| 5 | 6 | 7 | 8 | 9 | 10 | 11 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | |
| 12 | 13 | 14 | 15 | 16 | 17 | 18 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | |
| 19 | 20 | 21 | 22 | 23 | 24 | 25 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | |
| 26 | 27 | 28 | 29 | 30 | 31 | | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 28 | 29 | 30 | 31 | | | | |
| | | | | | | | 30 | | | | | | | | | | | | | | |



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12 Dose INH + RPT (3HP) Recommendations

- Equal alternative to 9 months INH in otherwise healthy individuals ≥ 12 years old + high risk for TB disease:
 - Close contact
 - Recent converter
 - Fibrotic changes on CXR
 - HIV not on ART, otherwise healthy
- Others considered on an individual basis if circumstances deem INH-RPT to be a better choice (likelihood of completion should be considered)

Recommendations for Use of an INH-RPT Regimen with DOT to Treat LTBI.
 MMWR / December 9, 2011 / Vol. 60 / No. 48

Villarino et al., *JAMA Pediatrics*, 2015

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INH and Rifapentine for 12 weeks (3HP)

- Efficacy was similar
- 82% in INH-RPT vs. 69% completion in standard therapy group
- Fewer adverse events in INH-RPT arm
- More hepatotoxicity in INH alone group
- More 'possible hypersensitivity' reactions in INH-RPT

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INH-RPT NOT Recommended

- Children < 2 years old
- HIV on ART
- Pregnancy, or likely to become pregnant during treatment
- Presumed INH or RIF resistance
- Prior adverse effects with INH or rifamycins

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Parent/caregiver education

- Use translator if needed
- Review reason for treatment
 - Future risks
 - School concerns
- Shared decisions
 - Duration and frequency
 - Ease of dosing
- Review regimens
 - 12 weekly big doses vs. 4 months of daily smaller doses
 - Rifampin: contact lenses, empty stomach, before bedtime?
- Review side effects
 - Rifampin: orange body fluid, drug interactions (OCP), rashes, liver toxicity, flu-like symptoms
 - INH: liver toxicity, peripheral neuropathy, rash

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Pyridoxine supplementation

- Rarely needed in children receiving INH
- Exclusively breastfed infants receiving INH
 - 1mg/kd/day
 - Not indicated if only the mother is taking INH
- Meat and milk deficient diets
- Nutritional deficiency
- Symptomatic HIV infected children
- Pregnant adolescents

<https://www.cdc.gov/tb/topic/treatment/pregnancy.html>; Loveday, et al. Int J Tuberc Lung Dis 2020

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What You Need to Know About Your Medicine for Latent Tuberculosis (TB) Infection

RIFAMPIN

You have been given medicine to treat your latent TB infection. You do not have TB disease and cannot spread TB to others. This medicine will help you **PREVENT** getting TB disease.

While on this Medicine:

- Tell your doctor or nurse if you have questions or concerns with the medicine.
- Go to your planned clinic visits.
- Discuss any alcohol use with your doctor. Alcohol use may cause side effects.
- Tell your doctor about all other medicines you are taking.
- Be sure to tell your other doctors that you are being treated for latent TB infection.
- Take all of your medicine as you were told by your TB doctor or nurse.
- Some people find that the medicine affects them less when taken with food.

Tips to Help You Take Your Medicine:

- Take your medicine at the same time every day.
- Set an alarm reminder for the time you should take your medicine.
- Ask a family member or friend to remind you.
- Use a pillbox.
- Put a reminder note on your mirror or refrigerator.
- Use a calendar to check off the day when you take your medicine.

Latent TB Infection Medicine Schedule:

(Providers: Indicate the appropriate schedule, days and number of pills)

| Medicine | Schedule | Number of pills per day | Length of time |
|----------|----------|-------------------------|----------------|
| Rifampin | Daily | | 4 months |

Your doctor may have you meet with a health care worker to take your medicine. This plan is called directly observed therapy (DOT).

IF YOU FORGET TO TAKE YOUR MEDICINE: If it is still the same day, take the dose as soon as you remember. Do not take 2 doses at the same time.

NOTES

Name of my doctor:
Name of my clinic:
Telephone number of my clinic:

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of Tuberculosis Elimination



Watch for these Possible Problems:

STOP taking your medicine right away **AND** call your TB doctor or nurse if you have any of the problems below:

- Less appetite, or no appetite for food
- An upset stomach or stomach cramps
- Nausea or vomiting
- Cola-colored urine or light stools
- Easy bruising or bleeding
- Rash or itching
- Yellowing skin or eyes
- Severe weakness or tiredness
- Fever
- Head or body aches
- Dizziness

NOTE: It is normal if your urine, saliva, or tears become orange-colored. Soft contact lenses may become stained.



What You Need to Know About Your Medicine for Latent Tuberculosis (TB) Infection

ISONIAZID

You have been given medicine to treat your latent TB infection. You do not have TB disease and cannot spread TB to others. This medicine will help you **PREVENT** getting TB disease.

While on this Medicine:

- Tell your doctor or nurse if you have questions or concerns with the medicine.
- Go to your planned clinic visits.
- Discuss any alcohol use with your doctor. Alcohol use may cause side effects.
- Tell your doctor about all other medicines you are taking.
- Be sure to tell your other doctors that you are being treated for latent TB infection.
- Take all of your medicine as you were told by your TB doctor or nurse.
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- Ask a family member or friend to remind you.
- Use a pillbox.
- Put a reminder note on your mirror or refrigerator.
- Use a calendar to check off the day when you take your medicine.

Latent TB Infection Medicine Schedule:

(Providers: Indicate the appropriate schedule, days and number of pills)

| Medicine | Schedule | Days | Number of pills per day | Length of time |
|-----------|--|------------------|-------------------------|----------------|
| Isoniazid | <input type="checkbox"/> Daily | Every day | | 9 months |
| | <input type="checkbox"/> Twice Weekly* | M T W Th F S Sun | | |

Your doctor may have you take vitamin B6 with your medicine.

Note: When Isoniazid is to be taken 2 times a week, it should be given by directly observed therapy (DOT).*

IF YOU FORGET TO TAKE YOUR MEDICINE: If it is still the same day, take the dose as soon as you remember. If the day has passed, skip the missed dose and take your next scheduled dose — do not take 2 doses at the same time.

NOTES

Name of my doctor:
Name of my clinic:
Telephone number of my clinic:

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of Tuberculosis Elimination



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- Nausea or vomiting
- Cola-colored urine or light stools
- Rash or itching
- Yellowing skin or eyes
- Tingling or numbness in your hands or feet

*Directly Observed Therapy (DOT)

You will meet with a health care worker to take your medicine. This plan is called directly observed therapy.

DOT can help you in several ways.

- The health care worker helps you to remember to take your medicine.
- You will complete your treatment as soon as possible.
- The health care worker will make sure you are not having problems with the medicine.



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What You Need to Know About Your Medicine for Latent Tuberculosis (TB) Infection

ISONIAZID and RIFAPENTINE

You have been given medicine to treat your latent TB infection. You do not have TB disease and cannot spread TB to others. This medicine will help you **PREVENT** getting TB disease.

Remember to Keep Your Weekly Visits:

You will meet with a health care worker weekly to take your medicines. This plan is called directly observed therapy (DOT).

DOT can help you in several ways.

- The health care worker helps you to remember to take your medicines.
- You will complete your treatment as soon as possible.
- The health care worker will make sure you are not having problems with the medicines.
- During your weekly meetings, this person can answer your questions. You can also talk about any concerns you have.

While on this Medicine:

- Tell your doctor or nurse if you have questions or concerns with the medicine.
- Go to weekly visits.
- Discuss any alcohol use with your doctor. Alcohol use may cause side effects.
- Tell your doctor about all other medicines you are taking.
- Be sure to tell your other doctors that you are being treated for latent TB infection.
- Some people find that the medicines affect them less when taken with food.

Latent TB Infection Medicine Schedule:

(Providers: Indicate the appropriate day and number of pills)

| Medicine | Schedule | Day | Number of pills per day | Length of time |
|-------------------------|-------------|------------------|-------------------------|---------------------|
| Isoniazid & Rifapentine | Once weekly | M T W Th F S Sun | | 3 months (12 weeks) |

Your doctor may have you take vitamin B6 with your medicine.

NOTES

Name of my doctor:
Name of my clinic:
Telephone number of my clinic:

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Division of Tuberculosis Elimination



Watch for these Possible Problems:

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- Fever
- Head or body aches
- Nausea or vomiting
- Cola-colored urine or light stools
- Easy bruising or bleeding
- Rash or itching
- Yellowing skin or eyes
- Severe weakness or tiredness
- Tingling or numbness in your hands or feet
- Dizziness

NOTE: It is normal if your urine, saliva, or tears become orange-colored. Soft contact lenses may become stained.



PATIENT INFORMATION

The 12-Week Regimen for Latent Tuberculosis (TB) Infection



You have been diagnosed with latent TB infection.

To treat your latent TB infection, take two medicines (rifapentine and isoniazid) once a week, for 12 weeks. It is important to take all of your medication. If you miss taking your pills for the week, call your doctor/clinic right away.

The 12-week regimen is not recommended for children less than 2 years old, pregnant women or women who expect to become pregnant during treatment, or some persons taking medicine for HIV.



What is Latent TB Infection?

'TB' is short for a disease called tuberculosis. TB is spread through the air from one person to another. People who become infected with TB germs, but do not feel sick have what is called latent TB infection. The reason a person does not feel sick is because the TB germs are latent, or inactive (sleeping), in their body. A person with latent TB infection has no symptoms and cannot spread TB germs to others.



Why Take Treatment for Latent TB Infection?

- A person with latent TB infection can have TB germs in their body for years before getting sick.
- Taking TB medicines is the only way to kill the TB germs in your body.
- Taking your medicines for latent TB infection can prevent you from developing TB disease in the future.



What are the Medicines You Will Take for 12 Weeks?

You will take two medicines (rifapentine and isoniazid) once a week, for twelve weeks. Your doctor may have you meet with a healthcare staff member to take your medicine, or they may tell you to take the medicine on your own.

One of the drugs, isoniazid, may cause tingling or numbness in hands and feet. Your doctor may add Vitamin B6 to your treatment plan to prevent this.

Before you start this treatment plan, tell your doctor if you are taking any other medicines, including birth control medications and medicine for HIV. Isoniazid and rifapentine may interact with certain medications, so it is very important for your doctor to know what medicines you are taking.

If you see another doctor, be sure to tell him or her that you are being treated for latent TB infection.



Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

www.cdc.gov/tb



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Treatment Adherence

- Monthly follow-ups
- Charts, phone reminders
- Young children
 - INH: crushed tablet (not suspension)
 - Rif: open capsule
 - Mix with spoonful of food
- Infants
 - Formula or breast milk via nipple
- DOT, school RN, pediatrician

HOW CAN I GIVE MY CHILD A PILL?



For babies and young children, the pill can be crushed.



The crushed pills can be dissolved in a teaspoon of water.

This can be mixed with a small amount of food such as apple sauce, mashed bananas, yogurt, or pudding.

TRY THESE TIPS TO HELP YOU REMEMBER TO GIVE YOUR CHILD THE MEDICINE:

- Give your child the medicine the same time every day.
- Have your child take the medicine before meals or before bedtime.
- Mark off your calendar every time your child takes a pill.
- Keep the medicine in a place where you cannot miss it, but out of the reach of children.

WHAT PARENTS NEED TO KNOW ABOUT TUBERCULOSIS (TB) INFECTIONS IN CHILDREN



PEDIATRIC TUBERCULOSIS DIFFERENCES

TB Disease by Age

| | Risk of disease following primary infection | | | Comments |
|------------|---|---------------------------|------------|---|
| | Disseminated tuberculosis/ tuberculosis meningitis | Pulmonary tuberculosis | No disease | |
| <1 years | 10-20% | 30-40% | 50% | High rates of morbidity and mortality |
| 1-2 years | 2-5% | 10-20% | 75-80% | High rates of morbidity and mortality |
| 2-5 years | 0-5% | 5% | 95% | .. |
| 5-10 years | <0-5% | 2% | 98% | "Safe school years" |
| >10 years | <0-5% | 10-20% | 80-90% | Effusions or adult-type pulmonary disease |

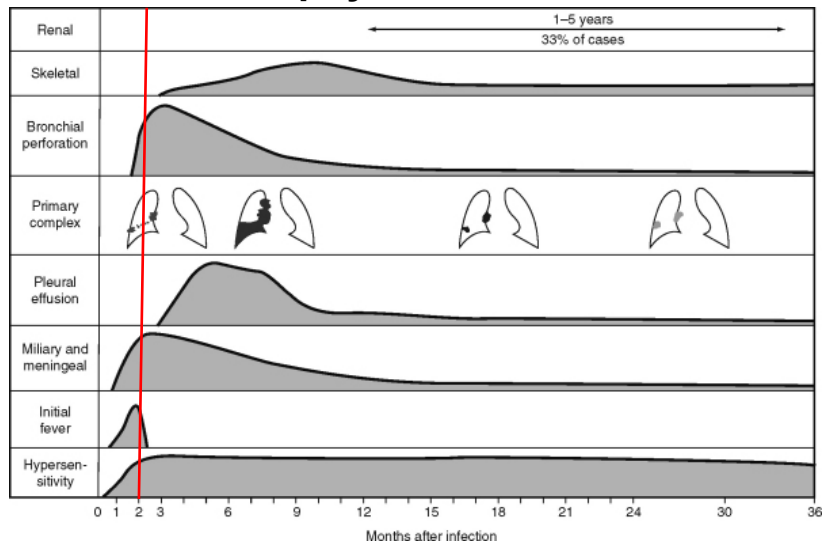
Adapted from reference 30.

Table 1: Risk of pulmonary and extrapulmonary disease in children following infection with *Mycobacterium tuberculosis*

Newton, et al. Lancet ID 2008

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Reason for Window Prophylaxis



From Starke Chapter 107 in Textbook of Pediatric ID 2009

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Treatment of Exposure Older than 5 years

- No evidence of active TB disease
- Normal immune system
- Normal physical exam
- Negative TST/IGRA

- Break infectious contact
 - Repeat TST in 8-10 weeks

- Monitor for signs of active TB disease

Treatment of Exposure Younger than 5 years

- | | |
|---|---|
| <ul style="list-style-type: none"> • No evidence of active TB disease • Normal immune system • Normal physical exam • Negative TST/IGRA • Negative CXR • Break infectious contact • Monitor for signs of active TB disease | <ul style="list-style-type: none"> • Initiate Window Prophylaxis <ul style="list-style-type: none"> – ASAP (Day of evaluation) – Presumptive LTBI treatment – INH or RIF (next slide) • Repeat TST/IGRA in 8+ weeks after contact is broken <ul style="list-style-type: none"> • Negative <ul style="list-style-type: none"> – Stop • Positive <ul style="list-style-type: none"> – Continue to complete LTBI Tx |
|---|---|

Choosing Window Prophylaxis

INH

- 10-15 mg/kg/day (Max 300)
- 100 and 300 mg pills
 - Ease of dosing
- Better CNS penetration
 - Preferred <12 months old
 - Consider <2 years old
- Longer duration for LTBI

RIF

- 15-20 mg/kg/day (Max 600)
- 150 and 300 mg capsules
 - Ease of dosing
- Shorter duration for LTBI
- Preferred >2 years old

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Evaluation of Window Prophylaxis

- Greater Houston area, 841 children <5 exposed from 2007-2017
- 10.6% not started on window prophylaxis
 - 85% already tested negative (missed opportunity)
 - 9% family refused
- 752 received prophylaxis
 - 97.1% INH
 - 2.7% RIF
 - No hepatotoxicity
- **37 (4.9%) converted**
 - Conversion associated with parental index case
 - Not associated with smear+ index case

Table 1. Characteristics of 752 children exposed to index tuberculosis patients, index patients, and index case *Mycobacterium tuberculosis* isolates, Houston, Texas, USA, 2007–2017

| Characteristic | Value* |
|--|---------------|
| Demographics | |
| Age, y, median (interquartile range) | 2.4 (1.2–3.6) |
| Sex | |
| F | 380 (50.5) |
| M | 372 (49.5) |
| Race/ethnicity | |
| Hispanic | 493 (65.6) |
| Black | 141 (18.8) |
| Asian | 78 (10.4) |
| White | 30 (4.0) |
| Biracial | 10 (1.3) |
| Residing in home of index patient | |
| Yes | 311 (41.4) |
| No | 441 (58.6) |
| Index patient microbiology | |
| Acid-fast bacilli smear positive | 513 (68.2) |
| Acid-fast bacilli culture positive | 680 (90.4) |

Cruz, A and Starke, J Emerg. Infect. Dis. 2019

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Use Source Case Data if Available

- Symptoms for how long?
- Cough for how long?
 - Exposure amount? Cohabitation - Don't use strict definition
- Chest imaging: Cavitory vs. non-cavitory? Miliary? Laryngeal?
- Sputum?
 - AFB smear results
 - Some data for highly smear positive cases too weak to cough vigorously
 - Cases not equally contagious over time
- When treatment started?
- CULTURE DATA

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MDR Contacts

- WHO guidelines for LTBI: Use Levofloxacin x 6 months “along with other TB medicines, such as EMB (or Ethionamide) if tolerated”
- Newer TB medications ?
 - No data for Bedaquiline in kids under 5 years
 - No data for Pretomanid in kids < 15 years
 - Data for Delamanid for >5 years and possibly (per WHO guidelines) 3-5 year olds (uncertain, how the capsules are absorbed if they need to be broken/crushed)
- New WHO operation handbook on TB (2022)
 - Preliminary dosing down to 3 kgs for both Bedaquiline and Delamanid
 - No peds data for Pretomanid
- Phone many friends

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PRACTICE CASES

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3-year-old without symptoms

- PPD placed at insistence of preschool
- 6mm induration at 48 hours
- Next steps?

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Table 3.74. Definitions of Positive Tuberculin Skin Test (TST) Results in Infants, Children, and Adolescents^{a,b}

Does she fit in here

Induration 5 mm or greater

Children in close contact with known or suspected contagious people with tuberculosis (TB) disease

Children suspected to have TB disease:

- Findings on chest radiograph consistent with active or previous TB disease
- Clinical evidence of TB disease^c

Children receiving immunosuppressive therapy^d or with immunosuppressive conditions, including human immunodeficiency (HIV) infection

Induration 10 mm or greater

Children at increased risk of disseminated TB disease:

- Children younger than 4 y
- Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition (see Table 3.75)
- Children born in high-prevalence regions of the world
- Children with significant travel to high-prevalence regions of the world^e
- Children frequently exposed to adults who are living with HIV, experiencing homelessness, or incarcerated, or to people who inject or use drugs or have alcohol use disorder

Induration 15 mm or greater

Children without any risk factors

Let's Say the IGRA Is Positive

- Evaluate for symptoms of TB
 - No fever
 - No respiratory symptoms
 - Normal activity, appetite, energy level
- Physical exam
 - No nodes
 - Clear lungs
 - Normal in all aspects
- CXR
 - Normal

- Initiate LTBI Tx
- Rifampin 15-20 mg/kg/day x 120 doses
 - OR
- Isoniazid 10-15 mg/kg/day x 180 or 270 doses

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3-year-old without significant history

- Parent admitted with 4 weeks of progressive cough and chest pain
- 3+ AFB smear positive
- RUL cavity

- What do you want to know?

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Index Case

- Smear 3+ and cavities
- 4 weeks of symptoms and close contact
- High risk of transmission

- PCR?
 - Confirm *M. tuberculosis*
 - Rifampin resistance?
- Culture data
 - Probably too soon
- Risks of resistance

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- Evaluate for symptoms of TB
 - No fever
 - No respiratory symptoms
 - Normal activity, appetite, energy level
- Physical exam
 - No nodes
 - Clear lungs
 - Normal in all aspects
- CXR
 - Normal
- IGRA or PPD negative

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- Initiate Window Prophylaxis
 - Rifampin 15-20 mg/kg/day OR Isoniazid 10-15 mg/kg/day
- Repeat original TB screening 8-10 week after contact broken
- If negative, stop treatment
- If positive, continue
 - Rifampin 15-20 mg/kg/day x 120 doses
 - OR
 - Isoniazid 10-15 mg/kg/day x 180 or 270 doses

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