

TB 101 Series

“Pediatric LTBI”

Dr. Kristina Feja
Chief, Pediatric Infectious Diseases
Saint Peter’s University Hospital
New Brunswick, NJ
Middlesex County TB Clinic

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Summary

- How children are different than adults?
- Who do we test?
- What test to use?
- Diagnosis of LTBI
- LTBI treatment options in children
- Parent education
- Treatment compliance
- Window prophylaxis

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Latest TB Incidence in U.S. (CDC)

(Updated 03/23/23)

Year	Number of Cases	Rate (cases/100K)
2022 (+ 5.4%)	8,300	2.5
2021 (-13%)	7,860	2.4
2020 (-20%)	7,174	2.2
2019	8,904	2.7
2018	9,006	2.8
2017	9,071	2.8
2016	9,242	2.9

From 60 reporting jurisdictions

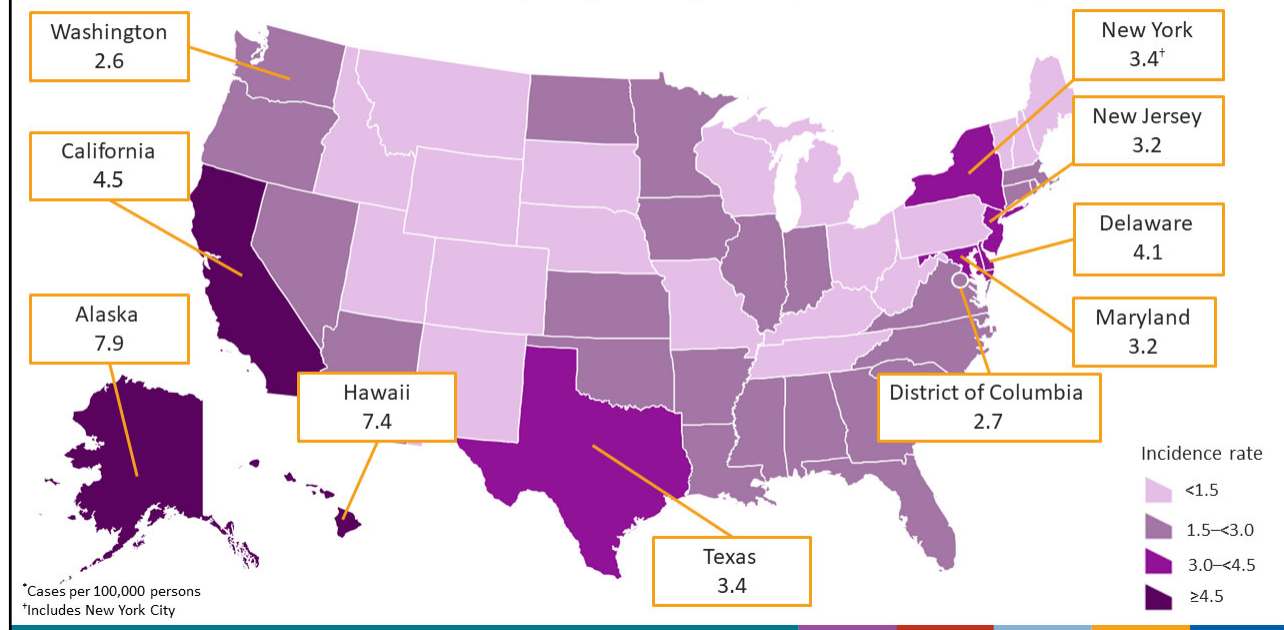
<https://www.cdc.gov/tb/statistics/default.htm>

- **Up to 13 million:** estimated LTBI cases
- Missed or delayed diagnosis
- Change in migration/travel

Characteristic	No. of TB cases* (%)		
	2021	2022	% Change 2021 to 2022
Total	7,874	8,300	5.4
Age group, yrs			
≤4	160 (2.0)	202 (2.4)	26.3
5-14	156 (2.0)	161 (1.9)	3.2

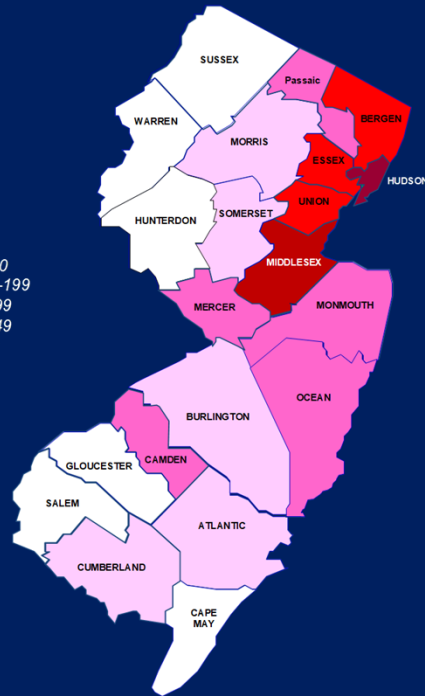
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TB Incidence Rates* by Reporting Area, United States, 2021



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Counted TB Cases New Jersey, 2016–2020



NJ DOH Frank Romano

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Latent TB Infection in children

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Diagnosis of Latent Infection

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



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Children ≠ small adults

LTBI in a child = public health sentinel event for recent transmission

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Risk Factors for Developing Disease

- Age < 4 years old
- Recent infection (within past 2 years)
- Medical conditions:
 - Hodgkin disease, lymphoma
 - End-stage renal disease
 - Diabetes mellitus
 - Malnutrition
- Immune suppression
 - HIV
 - Chemotherapy
 - Chronic steroid use
 - Other immune altering conditions (post-transplantation)
 - TNF –alpha antagonists (infliximab, etanercept)

AAP Red Book

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Progression to Disease

General population:

- 10% will develop disease during their lifetime
- 5% develop disease in first 2 years

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Risk of Tuberculosis 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

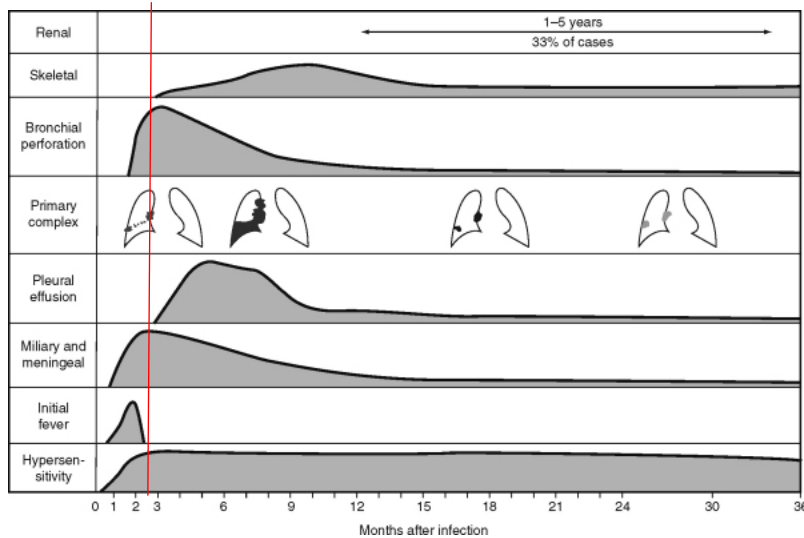
Adapted from reference 30.

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

Newton S, et al Lancet ID 2008 after Marais BJ, et al. Int J Tuberc Lung Dis 2004;
Pulmonary TB in adults and children, Miller & Wallgren; T. Nelson & Sons, 1939.

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Timetable of TB in Children after Wallgren



Tuberculosis. Starke JR, in Feigin, Cherry, Demmler, Kaplan, ed: Textbook of Pediatric ID 2009

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9 year old girl referred to Peds ID Clinic

- 10 mm TST (previously negative)
- Right hilar adenopathy on CXR
- Born in India, 4 y/o: moved to US, last visit to India > 2 yrs ago
- Otherwise healthy
- No symptoms
- Normal physical exam

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9 year old

Mother admitted to OSH with cavitary TB and AFB positive sputum on 4 drugs

- Chronic dry cough for months, failed antibiotics
- Started on 4 drug TB treatment as outpatient by pulmonology
- Vomiting, dehydration, LFT abnormalities - admitted x1 week

Father denies cough, fever, weight loss, night sweats, or other symptoms

- 10 mm TST
- CXR pending

4 year old brother sitting in office

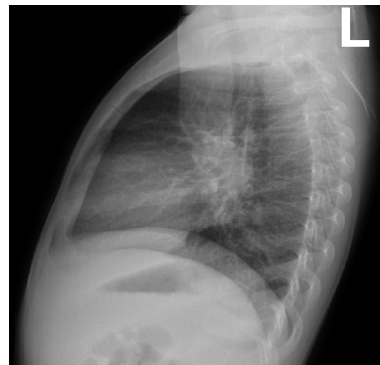
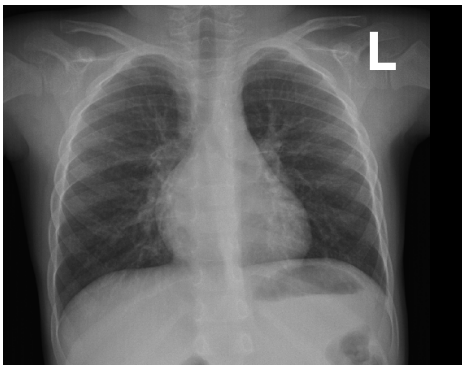
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4 year old brother

- Born in US, visited India > 2 yrs ago
- Completely asymptomatic
- PE completely normal
- TST negative 2-3 months ago

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4 year old



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Follow-up

Sister

- Started on 4 drugs next day
- 1 out of 4 sputum cxs positive
 - Pansensitive MTB
- Completed 6 mos of tx with DOT
- Did very well

Brother

- Started on 4 drugs next day
- Sputum cxs negative
- Completed 6 mos of tx with DOT
- Did very well

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Lessons Learned

- Always ask about other siblings or contacts
- Always look for siblings
- Ask about other families living in house

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Who should we test for TB?

Those children at risk for TB = exposed to TB

- Increased risk for LTBI
 - Close contact to person with TB disease
 - Born in endemic country
 - Travelled to endemic country (>2 weeks visiting friends/relatives)
 - Household contacts from endemic countries
 - Living with person with LTBI
 - Spending time with anyone who has: been in a prison or shelter, uses illegal drugs, or has HIV
 - Drinking raw milk or eaten unpasteurized cheese

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Validated risk assessment questions AAP

Has your child been exposed to anyone with TB?

If yes, ask:

- If the person had TB disease or LTBI, when the exposure occurred, and what the nature of the contact was.
- If exposed to someone with suspected or known TB disease: **Test + notify local health department**

Does your child have close contact with a person who has a positive TB test?

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Validated risk assessment questions AAP

Was your child born outside the United States?

If yes, ask:

- Where was your child born?
- All countries high risk **except**: US, Canada, Australia, New Zealand, Western/northern Europe

Has your child traveled to a high risk country?

If yes, ask:

- Where did the child travel, with whom did the child stay, and how long did the child travel? **2 or more weeks?**

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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"/> 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"/> 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/educationalmaterials/productfolder/PEDSTool.php>

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Children for whom immediate TST or IGRA is indicated (AAP Red Book)

- **Contacts** with confirmed or suspected contagious TB
- Children with **radiographic or clinical findings** suggesting TB disease
- Children **immigrating** from countries with endemic infection
- Children with history of significant **travel** to countries with endemic infection and substantial contact with indigenous people

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Who else to test? (AAP Red Book)

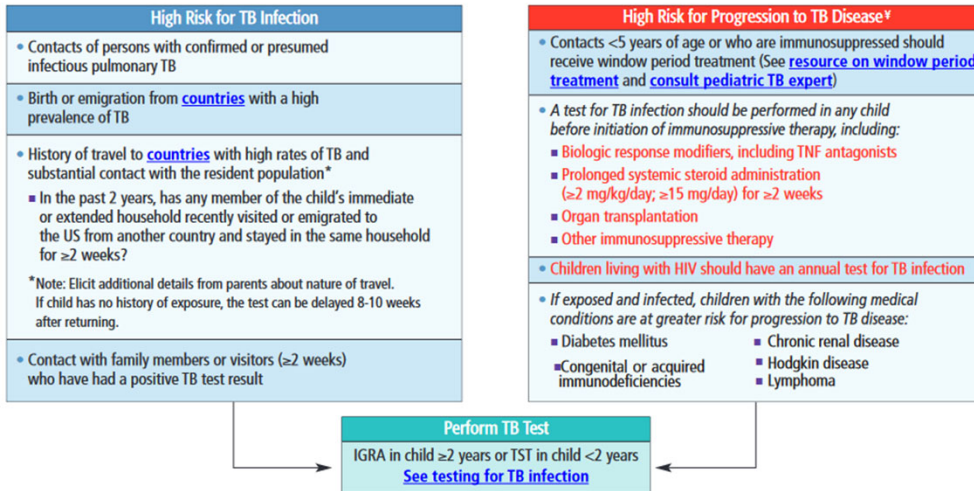
- Children infected with HIV (annually)
- Children at increased risk for progression to disease (if exposed)
 - Diabetes, chronic renal failure, malnutrition, immunodeficiencies
- Test prior to starting immunosuppressives, prolonged steroids, TNF-alpha antagonists, organ transplantation

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Pediatric Tuberculosis (TB) Risk Assessment Tool

Early diagnosis and appropriate treatment of children latent tuberculosis infection (LTBI) prevents morbidity and mortality. Young children with LTBI are at significant risk of progression to severe forms of TB disease. Infection is likely to be recent in children and adolescents and recent primary infection poses the greatest risk of progression. Consult a pediatric TB expert for evaluation of children who have symptoms of TB (e.g., cough, fever, night sweats, loss of appetite, weight loss or fatigue, failure to thrive, or an abnormal chest X-ray).

All children with a positive test for TB infection should be evaluated for TB disease before initiating LTBI treatment.



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Which test to use?

TST

- Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally
- Measure delayed-type hypersensitivity
- Reaction in 48-72 hrs
- Around since 1939



IGRA

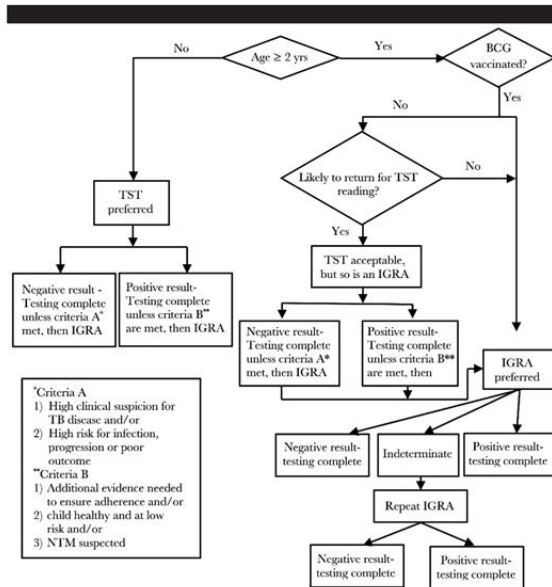
- Measure ex-vivo amount of interferon-gamma (IFN- γ) produced by T lymphocytes in response to stimulation with specific *M. tb* complex antigens
 - - not in BCG, most NTM
- Need fresh whole blood with viable wbc to incubate with controls and antigens
- Around since 2001
 - Ex: Quantiferon, T-Spot



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TB testing in children (Red Book)

Fig 3.16



< 2 years old: TST

≥ 2 y/o + BCG: IGRA

≥ 2 y/o + no BCG: TST or IGRA

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TST Interpretation: Positive or negative?

Induration of ≥5 mm is positive in:

- Children in close contact with known or suspected infectious case of TB
- Children with suspected TB disease:
 - Finding on chest radiograph consistent with active or previously active TB
 - Clinical evidence of TB disease
- Children who are immunosuppressed
 - Immunosuppressive therapy
 - HIV infection or immunodeficiency

Red Book

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TST Interpretation: Positive or negative?

- Induration of \geq 10 mm is positive in:
- Children at increased risk of disseminated disease:
 - Those < 4 years old
 - Those with concomitant medical conditions (eg, Hodgkin's disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition)

Red Book

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TST Interpretation: Positive or negative?

- Induration of \geq 10 mm is positive in:
- Children or adolescents with increased risk of exposure to TB disease:
 - Born in high-prevalence regions of the world
 - Travel to a country with high prevalence of TB
 - Frequently exposed to adults who are:
 - HIV-infected
 - Homeless
 - Users of illicit drugs
 - Incarcerated or institutionalized
 - Residents of nursing home

Red Book

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TST Interpretation: Positive or negative?

Induration of \geq 15 mm is positive in:

- Children \geq 4 years old without any risk factors

Red Book

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TST

False negative

- Infections
 - Viral illnesses (HIV, measles, varicella)
 - Bacterial (typhoid fever, brucellosis, typhus, leprosy)
 - Early TB infection (12 wk)
 - TB disease (meningitis, miliary, pleural)
 - Fungal (*Blastomycosis*)
- Live virus vaccines: Measles, Polio, Smallpox
- Concomitant medical conditions:
 - Metabolic abnormalities (chronic renal failure)
 - Malignancies (Hodgkin's disease, lymphoma, leukemia)
 - Sarcoidosis
 - Poor nutrition
- Drugs: Corticosteroids, chemotherapy
- Technical:
 - Newborns
 - Material: poor quality; inadequate dose (1 TU); improper storage (exposure to heat/light); expired
 - Not injected intradermally; read too early/late

False positive

- BCG vaccine
 - < 50% infants have a reactive TST at 9-12 months of age
 - 80-90% have nonreactive test by 5 years
- Exposure to NTM (eg, *M marinum*, *M kansasii*)
- Inexperienced or biased reader

Pediatrics 2004;114(Suppl):1175-1201.

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TST or IGRA is better?

sensitivity

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

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

specificity

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

Mandalakas 2011 IJTL

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TB test positive – what is next step?

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Diagnosis of Latent Infection

1. Positive tuberculin skin test (TST) or Interferon Gamma release assay (IGRA)
 2. Normal CXR or evidence of healed infections (calcified granuloma in lungs or calcification in lymph nodes)
 3. No signs or symptoms of TB disease
- 2 view CXR in <5 y/o
Read by pediatric radiologist
- Thorough history and Physical Exam



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LTBI treatment (CDC)

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)* and Rifampine (RIF)†	3 months	<u>Adults and Children aged 12 years and older:</u> INH: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT: 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 maximum <u>Children aged 2-11 years:</u> INH*: 25 mg/kg; 900 mg maximum RPT: as above	Once weekly	12
Rifampin (RIF)‡	4 months	<u>Adults:</u> 10 mg/kg <u>Children:</u> 15-20 mg/kg ^{ll} <u>Maximum dose:</u> 600 mg	Daily	120
Isoniazid (INH)* and Rifampin)‡	3 months	<u>Adults:</u> INH*: 5 mg/kg; 300 mg maximum RIF‡: 10 mg/kg; 600 mg maximum <u>Children:</u> INH*: 10-20 mg/kg; 300 mg maximum RIF‡: 15-20 mg/kg; 600 mg maximum	Daily	90

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LTBI treatment (CDC)

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)	6 months	Adults: 5 mg/kg Children: 10–20 mg/kg [†] Maximum dose: 300 mg	Daily	180
		Adults: 15 mg/kg Children: 20–40 mg/kg [†] Maximum dose: 900 mg	Twice weekly [†]	52
	9 months	Adults: 5 mg/kg Children: 10–20 mg/kg [†] Maximum dose: 300 mg	Daily	270
		Adults: 15 mg/kg Children: 20–40 mg/kg [†] Maximum dose: 900 mg	Twice weekly [†]	76

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Parent/caregiver education

- Use translator
- Review reason for treatment
 - 1 drug better than 4
 - 3- 4 months better than 6-9 months
- 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

- Exclusively breastfed infants
- Meat and milk deficient diets
- Nutritional deficiency
- Symptomatic hiv infected children
- Pregnant adolescents

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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 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

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

ISONIAZID

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- Go to your planned clinic visits.
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- Be sure to tell your other doctors that you are being treated for latent TB infection.
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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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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:



Watch for these Possible Problems:

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

- Less appetite, or no appetite for food
- An upset stomach or stomach cramps
- 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.

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



PATIENT INFORMATION

The 12-Dose 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-dose 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 compliance

- 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?



1



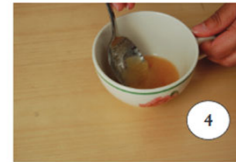
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For babies and young children, the pill can be crushed.



3

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



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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) IN CHILDREN



NEW ORLEANS
GLOBAL TUBERCULOSIS INSTITUTE

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Definitions

	TST/ IGRA	Physical Exam	CXR
Exposed	Negative	Normal	Normal
TB infection (LTBI)	Positive	Normal	Normal
TB disease	Positive	Abnormal/normal	Abnormal

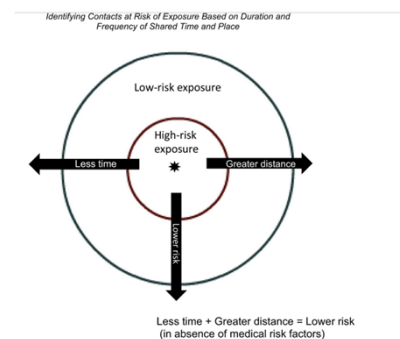
- Source case: adult with active contagious disease
- Window period: estimated interval between infection and detectable skin test reactivity / positive IGRA
- Window prophylaxis: treating patients at high risk for progression to active disease for TB infection even if evaluation is negative (during window period)
 - Children less than 5 years
 - Immunocompromised

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Ways of Finding TB Contacts

- Contact investigation around a source case
 - Source case: adult with active TB
 - Concentric circle
 - High priority: Household, Age <5 y, medical risk
 - Multiple rounds of questioning
 - Clues: children's shoes/toys in house
 - Multiple families
 - Illegal day cares

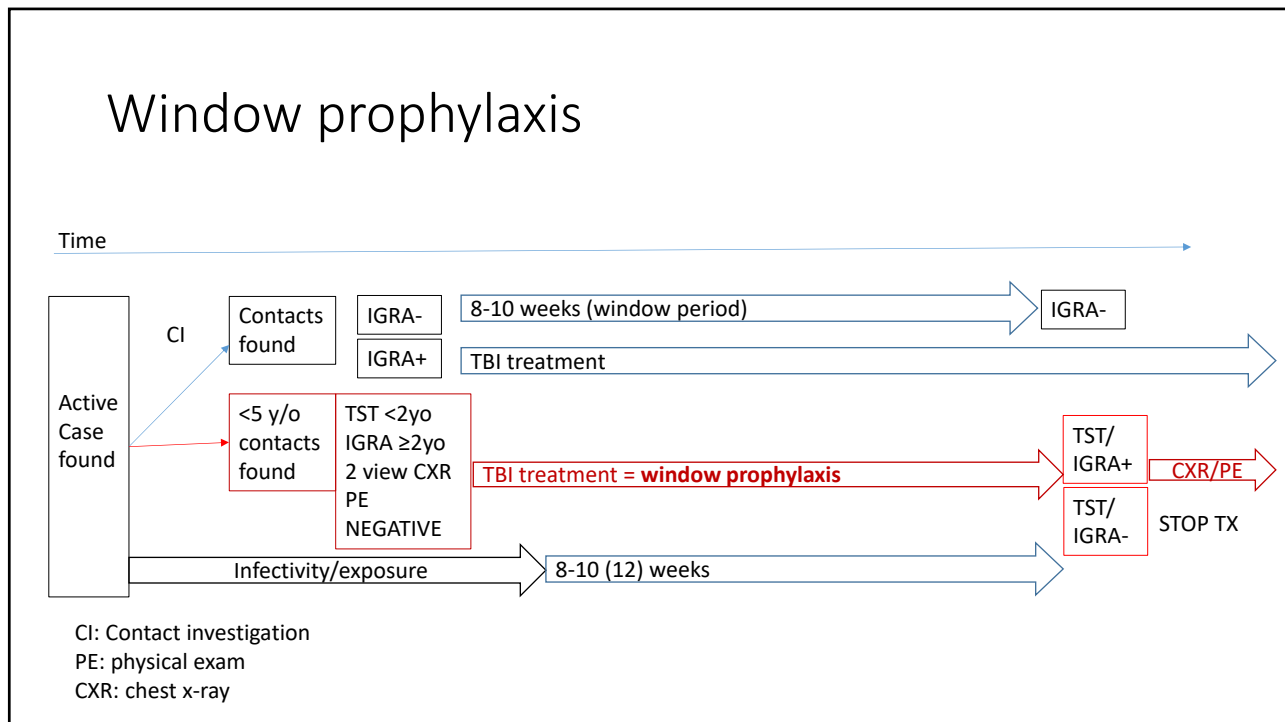
- Screening child - finding LTBI then screening the family to look for source case



Wolman et al. 2018
J Clin Tuberc Other Mycobact Dis

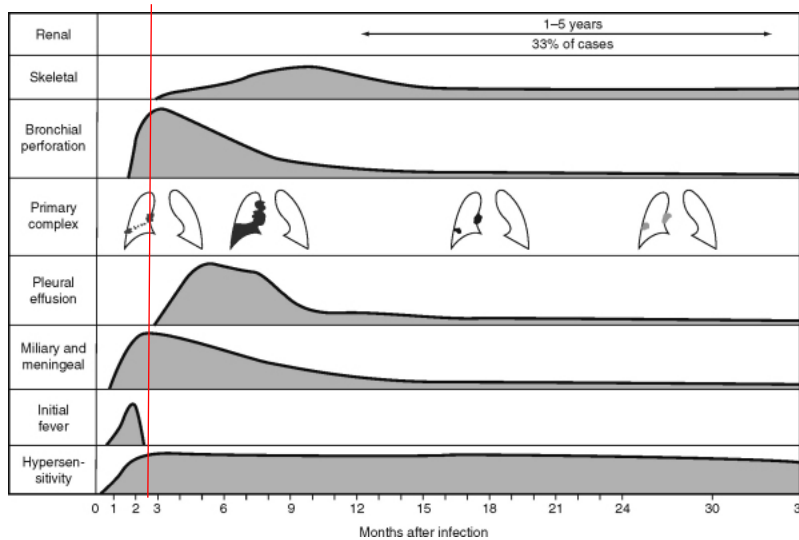
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Window prophylaxis



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Timetable of TB in Children after Wallgren



Tuberculosis. Starke JR, in Feigin, Cherry, Demmler, Kaplan, ed: Textbook of Pediatric ID 2009

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Things I want to know about source case

- Symptoms for how long?
- Cough for how long?
 - Exposure amount? Cohabitation - Don't use strict definition
- Chest imaging: Cavitory vs. non-cavitory? Miliary? Laryngeal?
- Sputums?
 - AFB smear results
 - Where done: Hospital? Non-induced at home? Induced at TB clinic?
 - Some data for highly smear positive cases too weak to cough vigorously
 - Cases not equally contagious over time
- When treatment started?

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Evolution of the AAP Red Book

- 2012: “For exposed contacts with impaired immunity (e.g., HIV infection) and **all contacts younger than 4 years, isoniazid therapy** should be initiated, even if the TST result is negative, once TB disease is excluded”
- 2018-2021: For exposed contacts with impaired immunity (e.g., HIV) and **all contacts younger than 5 years, treatment for presumptive LTBI** should be initiated, even if initial TST/IGRA is negative, once TB disease excluded... if TST/IGRA is still negative in an immunocompetent person, **isoniazid can be discontinued**
- 2021-2024: For exposed contacts with impaired immunity (e.g., HIV) and **all contacts younger than 5 years, treatment for presumptive TBI** should be initiated, even if the initial TST or IGRA result is negative, once TB disease is excluded.....If the TST or IGRA result still is negative in an immunocompetent person, **treatment can be discontinued**



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Which LTBI treatment to start?

- ~~Weekly INH and rifapentine → 12 weeks~~
- Daily Rifampin (15-20 mg/kg/day or 20-30 mg/kg/day) → 4 months
 - INH resistance
- Daily INH (10-15 mg/kg/day) → 9 months
 - Young infant ? – can't depend on accuracy of repeat testing
- Daily INH and Rifampin → 3 months

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Evolution of my practice

- INH in < 4 year olds (or Rifampin if INH resistant)

- < 2 year old: INH and finish with INH
- 2-4 year old: INH then switch to RIF (if can dose 15-20 mg/kg/dose with capsules)

- < 2 year old: INH – possibly finish with Rifampin
- 2-4 year old: RIF (unless can't dose Rifampin 15-20 mg/kg/dose)

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Window Prophylaxis, Houston 2007-2017

(Cruz and Starke, EID 2019)

- Retrospectively study of safety of INH in 752 TB-exposed children <5 years of age
 - Median age: 2.4 years
 - 41.4% resided in the home of the index patient
 - Index pt. Microbiology:
 - AFB smear positive: 68.2%
 - AFB culture positive: 90.4%
- Accepted by families - know what TB is
- Safe, well-tolerated: AE:7/752= 0.9%
 - Median time to AE: 5 weeks
- Conversion of TST: 37 children (4.9%)
- Conclusion: safe and effective!

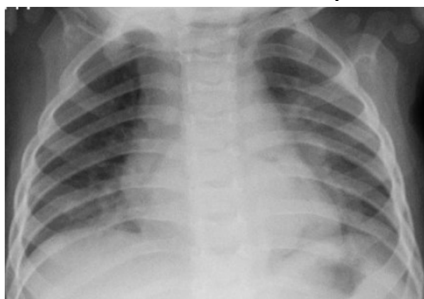
51

8 month old

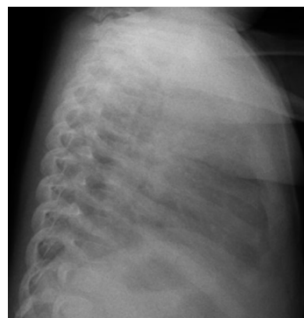
- Contact to father with pansensitive cavitary smear positive TB
- 3/3/21: 2 view CXR negative, QFT negative
- 4/2: ER for 104F, URI symptoms, decreased activity; CXR normal
- 4/7: admitted CXR perihilar opacities



4/2



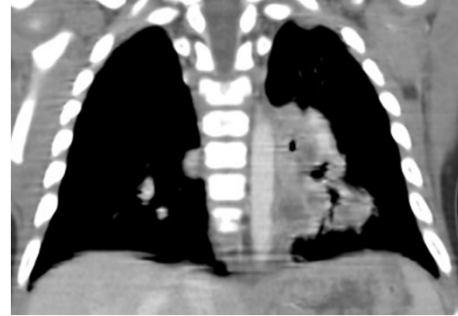
4/11



52

8 month old

- 4/9-4/11: Gastric aspirates sent
- 4/15:



- CT necrotic mediastinal LNs, consolidation - started RIPE
- 4/22: home from hospital on RIPE
- 4/23: TB clinic - looking great

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8 month old

- 4/28: wheezing in morning, 100.4F, increased cough, CXR improved
- 4/30: higher fevers, readmitted



4/30



5/3



5/4

- Admitted for 1 month on high doses of steroids and slow taper

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Lessons Learned

- Negative IGRA in < 2 year old does not rule out infection
- Window prophylaxis not given - **MISSED OPPORTUNITY**
- Preventable disease
- Need to educate all pediatric providers

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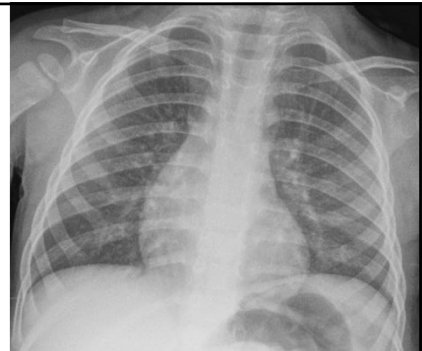
Polling Question What Would You Do?

- A) Start INH since Rifampin resistance detected
- B) Start PZA and ethambutol
- C) Start nothing because everyone tested negative in the house
- D) Start nothing because need more information on mother's sensitivities

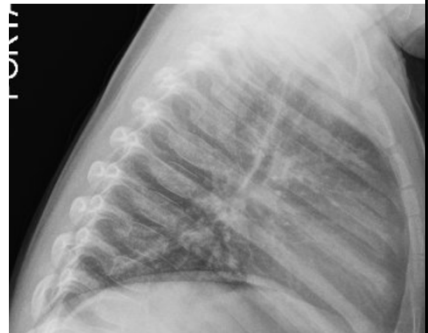
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Monday morning call to TB clinic

- 10/17: “I think I have TB”
- Mom with all classic symptoms
 - coughing since COVID in July
 - 4 previous rounds of TB treatment
- 9 month old and 3 y/o at home
 - 3 y/o has 103 fever, wheezing
- Mom: 4 + sputum, Genexpert +, Rifampin Resistant
- 10/21: TB clinic
 - PE normal
 - Both children CXR negative and TST/IGRA negative
 - Father and maternal grandparents all T-Spot.TB negative



10/17: 3 y/o: Peribronchial thickening



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MDR Contacts

- MDDR results on mother:
 - INH, RIF, EMB resistant, PZA pending
 - Sensitive to fluoroquinolones/injectables
- 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

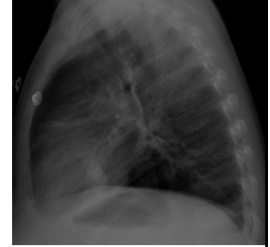
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MDR Contacts

- MDDR results on mother:
 - INH, RIF, EMB resistant, PZA pending
 - Sensitive to fluoroquinolones/injectables

11/4: TB clinic

- PE is normal, except URI symptoms
- Start Levo on both children
- 11/6: 3 y/o admitted with cough, respiratory distress
 - ER: Solumedrol
 - QFT: positive
 - Finished 6 months of Levo
- 9 month old remained negative- stopped window prophylaxis



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9/24/22

- Mother showed up in ER “worried about 3 year old’s fever because relative is being evaluated for possible TB”

- **MISSED OPPORTUNITY !!!**

Lesson Learned:

- Child with contact to anyone with possible TB → **ALERT ID/DOH!**

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Prevention of Tuberculosis in Children: Missed Opportunities

- Failure to find and appropriately manage adult source cases (case finding)
- Delay in reporting the initial diagnosis of TB
- Contact investigation interview failure
- Delay in evaluation of exposed children
- Failure to completely evaluate exposed children
- Failure to prescribe window prophylaxis
- Failure to maintain a contact under surveillance
- LTBI diagnosed; treatment not prescribed
- Failure to complete treatment for LTBI (Adherence)

Nolan RJ. AJP 1986

Mehta J, Bentley S. Am J Prev Med 1992

Dr. McSherry

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Take home points

 Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People™

Think. Test. Treat TB

- Need to think of TB
- Test only if risk/symptoms
 - Do appropriate testing by the right people
- 2 view CXRs needed in <5 y/o (review with Ped Radiologist)
- Get your own history
- TB in children is **sentinel event** for recent transmission
 - Look for source case! Contact investigations important!
 - Look for more siblings/contacts
- Treat all LTBI in children
- Childhood TB is preventable with window prophylaxis
- Optimize compliance: DOT, help from pediatricians, school nurses
- Use TB clinic resources

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