San Francisco Experience: Developing local guidelines for Latent Tuberculosis Infection (LTBI) in Pregnancy

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Why did we develop guidelines?

3 cases:

- Missed diagnosis of active TB in a pregnant patient
- Delayed diagnosis of TB meningitis in an infant whose mother was the TB index case
- Delayed CXR after +IGRA and concern for active TB



Why does this matter?

- TB during pregnancy presents greater consequences for mother and baby
- Pregnancy presents a unique opportunity to screen and treat

How did we create guidelines?

- Review of current guidelines for treatment recommendations in pregnancy (CDC, NTCA)
- Discussion with experts
- Literature review
- Discussion with our local obstetric group and PCP partners

SF TB Clinic Guidelines

Screen **all** at-risk pregnant patients with TST or IGRA

CXR for all TST+ or IGRA+

 For negative CXR, with shared decision making, consider LTBI treatment after second trimester

If pt. had CXR in prior 3 months and no sxs, no need to repeat CXR

Recommendations for Latent TB Infection Screening and Treatment during Pregnancy

The Centers for Disease Control and Prevention (CDC) and the National TB Controllers Association (NTCA) recommend that all pregnant persons with risk factors for active TB should undergo screening for TB infection¹. Babies born to persons with active TB may have lower birth weight and are at potential risk for congenital TB with associated high mortality. Additionally, infectiousness at delivery could expose both health care providers and the newborn.

TB testing with a tuberculin skin test (TST) in US-born or interferon-gamma release assay (IGRA) in non-US born is indicated in pregnant persons with the following risk factors:

- Non-US-born from a country with high TB endemicity
- HIV or immunocompromised status
- History of contact with a person with infectious TB disease during lifetime

See the California Department of Public Health TB Risk Assessment for details.

Positive TST or IGRA

Pregnant person with a positive TB test result should receive a medical evaluation, including a chest radiograph (CXR) with a lead shield. The CXR may be deferred until after the first trimester. The CXR should be done as soon as possible if the following are present:

- HIV or other immunosuppression
- History of recent contact with a person with infectious TB disease
- Documented TB infection test conversion in the past 2 years

In general, if person has had a normal CXR in the 3 months prior to medical evaluation and is asymptomatic, a repeat CXR is not necessary.

If the CXR has abnormalities suggestive of active TB disease per radiology report, refer to SFDPH TB Clinic as soon as possible. Contact us at 628 206-8524.

SF TB Clinic Guidelines

Decision to treat: shared decision

Recommendations for rifampin 600mg PO QD and recommendations regarding monitoring

<u>Treatment</u>

If the CXR is normal, the decision of whether to treat latent TB infection (LTBI) during pregnancy should be made on a case-by-case basis. Prenatal visits represent a unique opportunity for treatment of latent TB, as maternal health care benefits may be lost within a few weeks/months after delivery and many persons may only access medical care when pregnant. If treatment is deferred, a referral should be made to the primary care provider to treat the LTBI.

Recommendations to delay LTBI treatment during pregnancy have largely been based on increased risk of hepatotoxicity with isoniazid. 3HP has not been studied and should not be offered. Increase in risk has not been documented with rifampin-only based regimens.

Per NTCA guidance, SFDPH recommends persons with uncomplicated pregnancy can be treated for LTBI starting after the first trimester with rifampin 600 mg po daily x 4 months¹.

- If the person has risk factors (e.g., HIV or other immunosuppression, history of recent contact with a person with infectious TB diseases or is a documented convertor in the past 2 years), strongly encourage LTBI treatment as soon as possible.
- Educate on monitoring for liver toxicity (anorexia, new nausea, vomiting, abdominal pain, jaundice etc).
- Counsel on the presence of nitrosamines in rifampin. In general, per the FDA, nitrosamine impurities have been shown to be potential carcinogens in animal studies with high nitrosamine exposure over prolonged periods of time (e.g., the equivalent of years-decades). The benefits of treatment with short-course rifampin for latent TB far outweigh any potential risk from nitrosamine exposure².
- Once rifampin is started, obtain baseline and monthly liver function tests.
- If rifampin is contraindicated, considering deferring treatment until 3-6 months post-partum given risk for transaminitis with isoniazid and because there is little safety data on rifabutin.
- If LTBI treatment extends into the post-partum period, remind patient that rifampin is safe to take while breast-feeding for both infant and mother.

What's happened

- Shared our guidelines with local OB providers and created lines of communication
- Created Epic Smart phrase (note template) for OB providers
- Active tracking of consult questions and referrals for pregnant and post-partum patients with LTBI (17+ consults received)
- Treatment: one patient started on LTBI treatment with rifampin during pregnancy (stopped early due to increase in LFTs)
- 2 pregnancy referrals, now being treated post-partum
- Other referrals: treatment by PCP, preferred to wait until after treatment, lost to follow-up



Recommendations for Latent TB Infection Screening and Treatment during Pregnancy

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What's next

- Follow-up with partners
- Continue to track referrals for pregnant persons treated for LTBI
- Update our guidelines and review new research that becomes available

References

- 1. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2022. Available at URL: <u>https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/</u>
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- 3. Miele K, Bamrah Morris S, Tepper NK. Tuberculosis in Pregnancy. Obstet Gynecol. 2020 Jun;135(6):1444-1453
- 4. FDA Updates and Press Announcements on Nitrosamines in Rifampin and Rifapentine. Available at URL: <u>https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-nitrosamines-rifampin-and-rifapentine</u>. Updated Jan 28, 2021.

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