TB and Pregnancy

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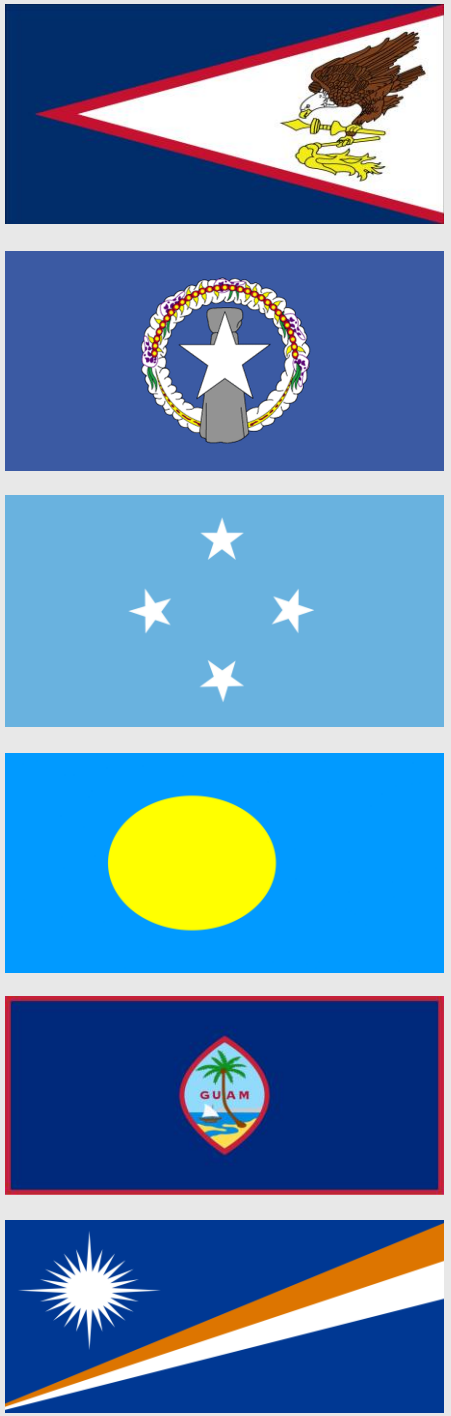
USAPI Regional TB Training 2024



Objectives

- Discuss the impact of TB on pregnancy
- Describe screening for TB and the workup of a pregnant person with suspected TB disease
- Discuss the treatment of LTBI and active TB in pregnancy
- Discuss implications of TB drugs on breastfeeding
- Review infection prevention considerations

The Impact of TB on Pregnancy

TB and pregnancy

- WHO reports 6-15% maternal mortality globally is associated with TB
- Adequate data on this topic is significantly lacking
- Up until recently, no definite increased risk of progression to TB disease, higher incidence of TB diagnosis in pregnant & postpartum
- WHO Global Tuberculosis Report 2024: increased risk of developing TB disease
  - Risk ratio in pregnancy: 1.3-1.4
  - Risk ratio in postpartum: 1.9-2.0
- Immunological changes in pregnancy may reduce ability to keep TB in a latent state
- Benefits of treatment of TB disease outweigh potential risks from TB drugs

TB and pregnancy

- Negative effects on the pregnant patient
  - Increased maternal morbidity (hospitalization, preeclampsia, eclampsia, anemia)
  - If patients living with HIV contract TB in the postpartum period, 2x more likely to die within the first year after birth compared to individuals who didn't develop TB
- Negative effects to the pregnancy
  - Increased miscarriage
  - Increased preterm birth
- Negative effects on the fetus or infant
  - Increased IUGR, SGA, LBW
  - Increased perinatal death
  - Increased risk of infant mortality
  - WHO reports 40-60% of infants under the age of 1 without HIV born to mothers with untreated TB disease will develop TB disease.

Slide adapted from: Maryam Mahmood MBChB

Screening and testing for TB in Pregnancy

Screening for TB in Pregnancy

- Identify risk factors for infection and disease
  - Recent contact with a person with TB disease
  - Living or working in high-risk areas
  - Incarcerated
  - Unhoused
  - Living in a high TB prevalence area
  - Regular travel to high TB prevalence area

Slide Credit: Maryam Mahmood MBChB

Screening for TB in Pregnancy

- Assess for symptoms of disease
  - Pregnant individuals living in an area with high TB incidence should be screened for symptoms of active disease every time they encounter a healthcare provider
  - TB symptoms may overlap with normal pregnancy symptoms
  - Symptom screening is generally the same as it is for non-pregnant individuals
    - Anorexia, weight loss, fever, night sweats, cough > 3 weeks, hemoptysis, fatigue, generalized weakness
    - Inadequate weight gain should be considered in addition to weight loss
- Physical exam
  - Evaluating for signs of pulmonary and extrapulmonary disease which manifest the same as they do outside of pregnancy

Slide adapted from: Maryam Mahmood MBChB

Diagnostic Evaluation for TB in Pregnancy

- TST and IGRAs are both acceptable
  - Obtain if symptoms are present, risk of exposure, or risk high risk of progression are present
  - Some evidence suggests that an IGRA performs better than a TST in pregnancy
  - Keep in mind that a negative TST or IGRA in pregnancy may carry a higher risk of false negativity
- Microbiology
  - Sputum collection or sample other sites of possible involvement
  - AFB smear, mycobacterial cultures, MTB PCR (GeneXpert)
  - May be more likely to have negative smears and cultures

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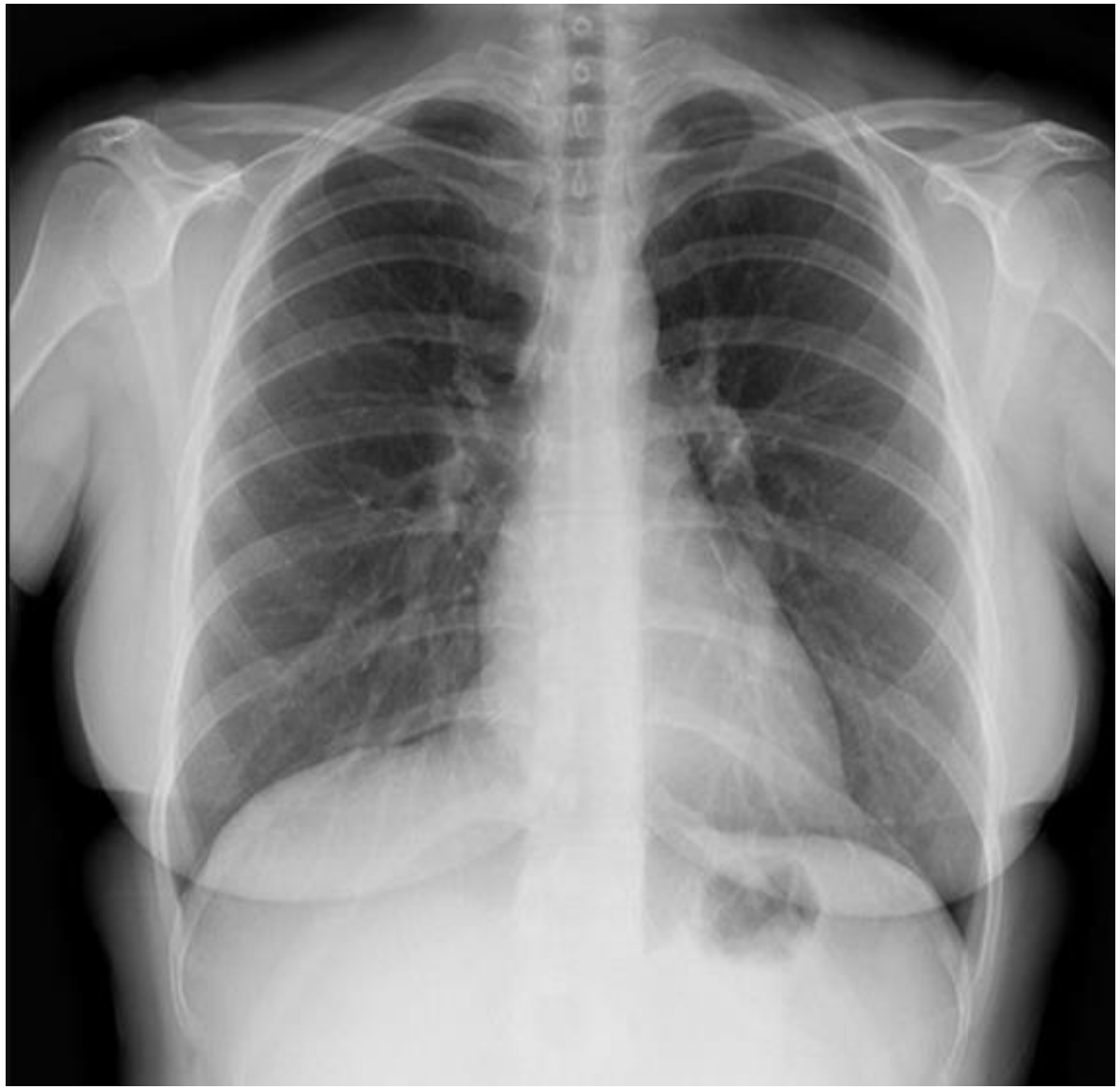
Diagnostic Evaluation for TB in Pregnancy

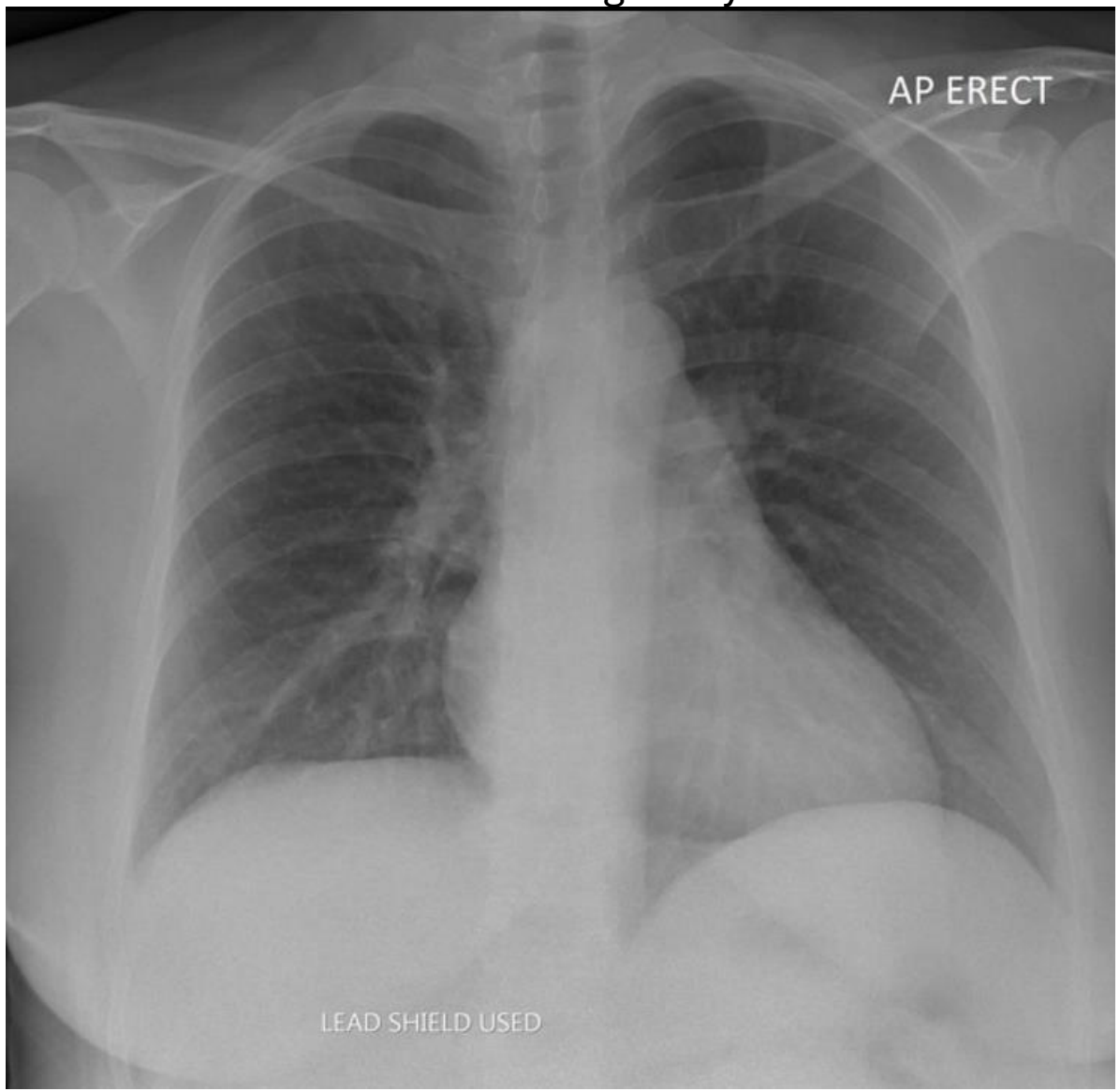
- Imaging – chest x-ray
  - It may be acceptable to delay chest x-ray until the second trimester in some situations
  - Pregnant people should not be denied necessary diagnostic procedures
    - CXR not associated with significant radiation to fetus (regardless of gestational age), can use shielding
  - Depending on stage of pregnancy, there are changes that may affect chest radiographs
    - Anatomical
    - Vascular
    - Lateral or lordotic views may be helpful in clarifying normal vs abnormal chest x-rays
  - Consider the possibility of atypical or subtle presentation

Normal Female CXR



https://www.radiologymasterclass.co.uk/gallery/chest/quality/chest-x-ray-normal-female#top_1st_img

CXR in Pregnancy



https://radiopaedia.org/cases/chest-x-ray-in-normal-pregnancy

Treatment of TB in Pregnancy

Who should be offered latent tb treatment in pregnancy?

- Mutual decision making
- Positive TST/IGRA in people without HIV
  - Recent exposure to pulmonary TB disease
  - TST or IGRA conversion within past 2 years
  - Immunocompromised
- Negative TST/IGRA with recent exposure to pulmonary TB disease
  - Immunocompromised
- People with HIV infection
  - Uncontrolled HIV infection
  - Recent exposure to pulmonary TB disease
  - TST or IGRA conversion within past 2 years

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LTBI regimens

4R	Rifampin daily for 4 months
3HR	Isoniazid and rifampin daily for 3 months
6H **9H**	Isoniazid daily for 6 or 9 months 9 months is preferred Consider in HIV (drug interactions)

- **Limited safety data for rifapentine – non-preferred in pregnancy**
- Possible increased risk of hepatotoxicity in pregnancy and early postpartum with INH

Slide adapted from: Maryam Mahmood MBChB

Monitoring on LTBI Treatment

- Baseline
  - Liver function tests (ALT, AST, bilirubin)
  - HIV, hepatitis B (HBsAg, HBcAb, HBsAb), hepatitis C screening
  - Evaluate for chronic liver disease, alcohol, other hepatotoxins
  - Patient counselling: Anorexia, nausea/vomiting, jaundice, dark urine, rash, paresthesia, fever > 3 days, abdominal pain, bruising/bleeding
- During treatment
  - Monthly clinical symptom evaluation, examination
  - Monthly liver function tests
  - More frequent monitoring if baseline abnormal liver function tests or liver disease

Slide Credit: Maryam Mahmood MBChB

Drug Susceptible TB Disease Treatment

- WHO: no changes in regimen for drug susceptible TB, generally 6 months of treatment
- No changes to regimen with HIV infection
- DC EMB when DST is received
- B6 supplementation

Isoniazid	Safe to use during pregnancy Monitor for symptoms/signs of liver toxicity Consider monthly LFTs (esp. if known liver disease) Administer with pyridoxine (B6) supplements
Rifampin	Safe to use during pregnancy Consider vitamin K supplements to prevent anemia in newborn
Pyrazinamide	Included in WHO recommended treatment regimen If not used, must extend to 9 months Monitor for symptoms/signs of liver toxicity Consider monthly LFTs (esp. if known liver disease) Individualized use, shared decision making (HIV, severe, EPTB)
Ethambutol	Safe to use during pregnancy

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Monitoring on Treatment of TB Disease

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  - Liver function tests (ALT, AST, bilirubin)
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Slide Credit: Maryam Mahmood MBChB

Drug Resistant TB

- Limited data – benefits still outweigh risks
- Pregnant people excluded from BPaL and other RR/MDR-TB trials
- Will have to be individualized based on drug sensitivities and mutual decision making
- Avoid aminoglycosides
- No data to say specifically that one regimen is better tolerated or more efficacious in pregnancy
- Expert consultation

Slide adapted from: Maryam Mahmood MBChB

Drug Resistant TB

- WHO conditional recommendation for a 9 month all oral regimen (one of which is safe in pregnancy)
- 9-month oral regimen in pregnancy
  - 4-6 months: BDQ (6m) – Lzd (2m) – Lfx/Mfx-Cfz-Z-E-Hh
    - Initial phase: 4 months of Lfx or Mfx, Cfz, PZA, EMB, high dose INH (10-15 mg/kg/day) with initial 2 months LNZ, and 6 months of BDQ
    - Continuation phase: 5 months Lfx/Mfx-Cfz-Z-E
  - Exclusion
    - FQL resistance
    - Extensive disease
    - Severe EP disease (TB meningitis, miliary, bone or joint, pericardial disease)
  - Inclusion populations
    - Children
    - HIV
    - Pregnant women
  - <1 month of exposure to BDQ, clofaz, LNZ or r/o of resistance with >1 month of exposure

Drug Resistant TB

- Additional considerations with this regimen
  - Sputum positive at 4 months, extend initial phase to 6 months
  - BDQ can be extended to 9 months if the initial phase is extended to 6 months
  - The regimen is not recommended when there are any signs of optic neuritis or peripheral neuropathy
  - Levofloxacin may be used instead of Moxifloxacin
  - If full dose (600 mg) of LNZ is not tolerated for the first 2 months, switch to a new regimen
  - If BDQ, Lfx/Mfx, LNZ, of Cfz is stopped early, switch to a new regimen
  - If PZA or EMB is not tolerated one of them (not both) can be dropped during the continuation phase without a regimen switch

Breastfeeding Considerations & Infection Prevention

Breastfeeding

- Encouraged if on first line therapy for at least 2 weeks
- Pyridoxine recommended for all breastfeeding persons on isoniazid
- Dose immediately after feeding and before infant's longest sleep period to reduce drug levels in the breastmilk
- Breastfeeding is not effective treatment for TB disease or LTBI in infant

Slide Credit: Maryam Mahmood MBChB

Isoniazid	Present in breastmilk, unlikely to exceed recommended infant doses
Rifampin	Low breastmilk concentrations (modeling studies), likely low infant exposure. May cause breastmilk discoloration.
Pyrazinamide	Low measured breastmilk concentrations, unlikely to exceed recommended infant doses
Ethambutol	Low measured breastmilk concentrations, unlikely to exceed recommended infant doses

Slide Credit: Maryam Mahmood MBChB

Infection Prevention in TB Disease

- Mother should wear a mask until no longer infectious
- No difference in risk of transmission while pregnant if on effective TB therapy
- Standard infection prevention practices during pregnancy, labor, delivery and postpartum period
- Avoid separating parent and newborn
- Inappropriate infection control practices can increase stigma, lead to adherence issues

Slide adapted from: Maryam Mahmood MBChB

In Summary

- TB disease causes poor health outcomes in all aspects of pregnancy
- Treatment of TB infection can be done during pregnancy and prenatal care provides a unique opportunity to complete LTBI treatment
- Benefits of treatment of active disease in pregnancy outweigh risks
- Research about this topic is lacking and many recommendations are based on limited data