No disclosures

Objectives:
Assess the risk of transmission to a neonate following an exposure in a NICU and identify those who will need evaluation
Evaluate a neonate for evidence of TB disease following a known exposure

Perinatal Tuberculosis
- Like other infections of the newly born, TB can be
  > Congenital – acquired in utero
    • Hematogenous acquisition, often during maternal bacillemia
    - Primary or disseminated TB in mom most common
    • Tubercle can rupture into amniotic fluid and baby can swallow or “inhale” infected fluid into the lung
  > Natal – acquired during the birth process
    • Late swallowing or inhaling of amniotic fluid or urogenital secretions
  > Postnatal
    • Inhalation of tubercle bacilli when mom or another caregiver has contagious pulmonary/laryngeal TB
Perinatal Tuberculosis

- Like other infections of the newly born, TB can
  - Have very non-specific signs and symptoms
    - Fever
    - Respiratory distress
    - Chest radiographic changes
    - Non-specific lab abnormalities
    - Enlarged liver / spleen / lymph nodes / rashes
  - Be difficult to diagnose
  - Associated with an asymptomatic mom
  - Can be diagnosed shortly after delivery or weeks to months later

Congenital Tuberculosis

- True congenital TB is not always easy to discern from post-natal acquisition

- Cantwell criterion: proven TB plus one of:
  - Lesions in the first week of life
  - Primary hepatic complex or caseating hepatic granulomas
  - Tuberculous infection of the maternal placenta or genital tract
  - Exclusion of possibility of postnatal transmission

Ann’s first TB patient

- J -
  - Full term baby 3 kg  24 year old G3 Latina
  - Thick meconium, but Apgars 91 and 95
  - Two days of age, fever, WBC 27.5; Plt 96
  - Bacterial and viral cultures negative
  - Increasing lymphadenopathy, hepatomegaly
  - Splenomegaly, irritability, pneumonitis.

  - DOL #10, mom came to the nursery
  - Held her head as she sat down
  - Mom Dx with TB meningitis - *M. bovis*
  - Baby’s gastric aspirates were smear positive

Congenital Tuberculosis

Evaluation — baby with history concerning for congenital TB or mother with TB disease during pregnancy

- Good physical exam
- Chest radiograph
- Gastric aspirates for smear and culture if ANY abnormality
  - > nearly 100% yield
- Endotracheal aspirates if ANY abnormality
- CSF, pleural fluid, middle ear fluid analysis if ANY abnormality
- Other labs not helpful (BUT: rule out TORCH, bacterial infections)
- TST sometimes positive

Evaluation - Mom

If mom not previously diagnosed with TB:

- History & PE
- TST / IGRA
- exposure history;
- Chest radiograph;
- cervical / endometrial
  - biopsy sampling
  - smear / PCR / culture
- Placental culture; pathology for any pregnant mom with TB
  (lots of placentas have granulomata – just increases risk if+)

<table>
<thead>
<tr>
<th>Type of Maternal TB (baby with congenital TB)</th>
<th>Of 170 cases reviewed N (%)</th>
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<tbody>
<tr>
<td>Miliary TB</td>
<td>53 (31%)</td>
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<tr>
<td>Genital or placental TB</td>
<td>45 (26%)</td>
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<tr>
<td>TB Pneumonia</td>
<td>22 (13%)</td>
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<tr>
<td>TB meningitis</td>
<td>12 (7%)</td>
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<tr>
<td>Pulmonary TB</td>
<td>22 (13%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (5%)</td>
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<th>Time to diagnosis of mother</th>
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<tr>
<td>Pre-partum</td>
<td>36 (21%)</td>
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<tr>
<td>Post-partum</td>
<td>121 (71%)</td>
</tr>
</tbody>
</table>
What if:

- Mom has TB disease and the baby has no evidence of congenital TB:

  If mom has well documented smear / culture conversion and there are no other cases of TB disease in the baby’s environment -

  **NO TREATMENT of the baby**

What if:

- Mom has TB disease and the baby has no evidence of congenital TB:

  If mom has recently started treatment and has not yet had time to convert sputa - or there is any concern for other cases of TB disease in the environment – after congenital TB disease is “ruled out,” start INH “prophylaxis” and vitamin B6 if breastfeeding

  - After three months, reevaluate and decide if mom might have been contagious after the baby was born. If so, continue the INH for nine months and perform a TST at 1 year of age for new baseline
  - If after three months, you see that mom, in fact had converted her sputa before delivery (cultures negative), you could perform a TST (knowing it’s not perfect) and if negative, stop the INH
  - If equivocal maternal sputum status at delivery, could TST baby at 6 months and stop if TST negative.

What if:

- Mom is on INH and is breastfeeding

  - Keep the baby’s dose close to 10 mg/kg/dose (will get some in the breastmilk). Baby’s often tolerate the liquid INH if tablet size is not convenient.
  - Use ½ tablet of 25 mg Vitamin B6
  - Reevaluate INH dose regularly as the baby grows
What if:

- Mom has TB disease which has not yet been treated (or treated so recently that she is still clearly contagious) and the baby has no evidence of congenital TB:
  - Separate mother (or other source) and baby
  - Treat the baby with INH or rifampin (if INH R, Rif S) once TB disease has been ruled out
  - Use B6 if baby breastfeeding
  - Reunite ASAP

- Consider BCG for untreatable contacts or MDR

Congenital Tuberculosis

- High index of suspicion
- Watch baby serially for evidence of congenital TB over months
  - At least twice monthly follow up looking for growth, fever, feeding, activity, work of breathing, hepatosplenomegaly, lymph nodes, rash
- Baby will rarely be symptomatic at birth
  - Theory is that low oxygen environment in utero keeps mycobacterial growth minimal. Markedly increased growth after delivery
- Treat with four drugs if evidence of active TB

Congenital TB after in vitro fertilization

- Genital tuberculosis is a common cause of worldwide infertility
- Congenital TB would be much more common if those patients weren’t frequently infertile
- Women with urogenital TB are frequently asymptomatic
- 47% - 76% of women with genital TB are infertile
- In developing countries, genital tuberculosis represents 2-21% of causes of infertility
- In India, using molecular diagnostics & multiple specimens 56-78% of infertile women have been found to have MTB positive endometrium or menstrual blood.
### Congenital TB after in vitro fertilization

- 11 cases of congenital TB after IVF have been reported
  - 2005 Turkish woman underwent IVF in France
    - Baby diagnosed with congenital TB at almost 3 months of age
    - Mother diagnosed with genital / CNS / pulmonary TB 2 months after delivery
  - 2009 report Turkish woman diagnosed with genital TB after delivering twins prematurely
    - Twins were screened and found to have pulmonary TB
  - 2013 US report of 5 babies born to Indian moms with congenital TB
    - All underwent IVF in New Jersey
    - One mom had suspected clavicular TB in the past and declined treatment. Subsequent TST was negative; not reevaluated before IVF
      - Twins diagnosed with *M. africanum* congenital TB
    - Another mom had tubal abnormalities; TST positive; calcified nodes; no TB Tx
      - Twins diagnosed after mom found to have endometrial TB

### Perinatal TB infection

- Much more common than congenital TB
- More pulmonary, miliary and disseminated disease
- Source case
  - Mother
  - Father
  - Other household
  - Nursery contacts
- High risk / rapid progression with HIV co-infection

### TB exposures

- Like all TB exposures, variables predict transmission
  - Smear / cavitary status of source case
  - Duration of exposure
  - Volume of shared air / air exchange rate / pattern
  - Virulence of the individual strain
  - Cough hygiene of the source case or aerosolizing procedures
- Nursery / NICU exposures
  - Infants with TB disease
  - Mother / visitor with TB disease
  - Health care worker with TB disease
- "Young children with TB are not contagious"
  - Except when they are
    - 13 cases of < 10 yr old transmitters reported before 2006; 5 were < 1 yr of age and 3 were congenitally infected
Nursery Exposures – congenital TB

  > 90 babies evaluated – no evidence of TB disease / infection
- 1998 Lee CID 27:474-7
  > Babies in the same room as premature infant with congenital TB on oscillating ventilator for > 24 hours screened and treated with INH.
  > None converted their TST
  > 4 of 27 visitors were TST positive / CXR negative
  > 2 direct care nurses converted their TST / CXR negative
- 2002 Laartz Int Contr & Hosp Epi 23:573-9
  > Premature infant dx congenital TB; required oscillating ventilator
  > All infants in the NICU during ventilation were evaluated with TST, CXR and Rx INH. No TB cases or TST positive
  > 226 staff and visitors evaluated – no proven transmission

- 2004 Mouchet Infect Contr Hosp Epi 25:1062-6
  > Premature infant dx with congenital TB at DOL 102
  > 139 HCW exposed
  > 6 HCW converted among 50 with close contact; no TB disease
  > Of 34 infants; 10 received INH; No TST conversions or disease

  > Premature infant diagnosed with congenital TB post-mortem
  > 107 infants evaluated; Rx with INH and no TST conversion
  > 1 infant developed TB disease – thought to be due to contaminated pulmonary equipment (not in same room as source case)
  > 3 HCW converted their TST
  > Ventilatory equipment, anesthesia supplies and feeding tubes have previously been implicated in TB transmission

- 2010 – Winters Int J Tub Lung Dz 14:1641-3
  > Premature infant managed in three hospitals before dx of congenital TB
  > Infant on oscillating ventilator
  > Two HCW converted TST; no TB disease
  > 9 infants and 10 visitors TST negative
Nursery Exposures - HCW

  > Nurses aid with pulmonary TB
  > 259 low risk infants skin tested / followed. None converted their TST
  > 139 higher risk infants skin tested / treated with INH. None converted their TST
- 1976 Steiner Am Rev Resp Dis 113:267-72
  > Nurses aid with pulmonary TB
  > 2 infants who had been in the nursery developed miliary TB
  > 1647 infants skin tested / evaluated – all neg TST / no evidence of disease
- 1978 Burk South Med J 71:7-10
  > Nurse with pulmonary TB
  > 514 infants evaluated – none converted their TST or developed TB disease

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Nursery Exposures - HCW

- 1998 Kim Pediatric Rad 28:836-40
  > 5 Korean babies 2 – 3 months of age were diagnosed with culture proven TB disease
  > Source was likely nursery exposure
  > 3 of 184 "exposed" infants developed MDR-TB
  > Median hospital stay 5 days
  > Dis TB 4 - 15 months after birth
  > One mother also diagnosed with MDR 12 months later
  > ? Source - HCW or non-compliant adult patient

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Nursery Exposures - HCW

- 2003 CDC MMWR 12/23/2005 1280-3
  > Nurse diagnosed with TB disease
  > 78% of coworkers had prior positive TST and none tx for LTBI
  > Remaining co-workers all TST negative
  > Extensive outreach found only 36% of 860 infants and 24% of 900 women
  > 5 of 227 infants were TST positive (one had received BCG)
  > 9 of 216 women converted TST (assoc with foreign birth; not contact with RN)
- 2008 Ohno J Infect Chemother 14:66-71
  > Nurse developed 3+ smear pos TB
  > 1 mother and 2 co-workers could have been infected
  > Babies received window prophylaxis and all TST neg
- 2011 Borgia Euro Surveill 16:pii=19984
  > Italian nurse diagnosed with pulmonary TB
  > 1 infant diagnosed with TB disease
  > 9% of infants had positive QFT-TB; none positive TST and no TB disease
Nursery Exposures – mother

- 2006 Berkowitz Infect Contr Hosp Epi 27:604-11
  - HIV infected, smear negative mom diagnosed with TB disease
  - Decision model developed to compare use of INH prophylaxis for exposed infants with no prophylaxis
  - Risk of infection estimated at 1 in 1000 based on Light, Steiner, Burk, Myers and Spark reports
  - Prophylaxis indicated if risk of infection > 2/10,000
  - $930,000 / death prevented for SAT
  - $21,000,000 / death prevented for DOPT

Teaching points

- Most babies born to moms with TB infection or disease will not be affected
- Watch for congenital AND perinatal infection
- Gastric aspirates have great yield in babies
  - Gastric aspirate video and instructions – Nicholas Loeffler
  - http://www.currytbcenter.ucsf.edu/pediatric_tb/resources.cfm
- Use INH prophylaxis liberally once active disease has been ruled out
- Use B6 if breastfed baby
- INFECTION CONTROL

Teaching points

- Congenital TB is very rare
  - Mom’s with 1st, disseminated or asymptomatic (genital) TB
  - Pregnant women should be screened for TB risks
  - Infertile women should be evaluated for TB risks
  - TB should be treated before in vitro fertilization
  - Congenital TB should be considered:
    - High risk population
    - Lung disease not responding to anti-bacterial therapy
    - Hepatosplenomegaly, lymphadenopathy, persistent fever, etc.
Teaching points

- TB has been transmitted in nurseries and NICUs from:
  > Babies with congenital tuberculosis
  > Health care workers
  > Moms
  > Unknown source (? Other adult patients or visitors)

- Contact investigation should be customized
  > Multidisciplinary team convened
  > Closest contacts and highest risk contacts prioritized
  > Risk of transmission assessed based on smear positivity, cavitation, duration of symptoms, ventilation, duration of exposure, etc
  > Window prophylaxis should be considered if significant risk discerned

Thank you!