Learning Objectives

At the end of this presentation, the participant will be able to:

1. Discuss national and local epidemiology of congenital syphilis, and factors contributing to a rise in cases
2. Understand prevention, clinical manifestations, and treatment of congenital syphilis
3. Interpret and manage results from reverse sequence serology testing

Risk factors

- Late or no prenatal care
- HIV
- Geography: known hot spots (e.g., Baton Rouge, Baltimore, metropolitan areas, especially in the South)
- Other STIs
- Race: African-American
- Low socioeconomic status
Adolescents and adults
• **Primary** often unnoticed, highly infectious, lasts 1-5 weeks
• **Secondary** may overlap first stage; condyloma lata and mucous patches are highly infectious. Lasts 2-6 weeks
• “Early non-primary non-secondary” (formerly “early latent”) vs. unknown duration/late: 1 year cutoff

![Graph showing congenital syphilis rates for Bexar County, Texas, and United States, 2013-2017]

- Rate of congenital syphilis in Bexar County has been higher than the US and TX since 2013.
Early or late syphilis?
- Unequivocal history of ulcer/rash?
- When did patient last have blood drawn for STI testing?
- Err on the side of late/unknown

Treatment
- Primary, secondary, early latent
  - Bicillin PCN L-A 2.4 μg IM weekly x 1
- Late latent/unknown duration
  - Bicillin PCN L-A 2.4 μg IM weekly x 3 doses

PCN allergy
- No alternative to penicillin in pregnancy
- Skin allergy testing, if possible, for future reference
- Desensitization in-house:
  - Oral dosing safer, easier, cheaper than IV
  - If weekly doses—repeat desensitization each time

Treatment: Jarisch-Herxheimer
- Fever, myalgia, worsening rash—not a PCN allergy!
- From endotoxins released by dying spirochetes
- Almost all primary patients & at least half of others < 1 year
- Starts in a few hours, lasts at most 24 hours
- In pregnancy: contractions (42%), decelerations (39%), decreased fetal movement


Treatment: Missed Doses
- Non-pregnant adults
  - Restart if > 14 days—but maybe ideal is > 9 days
- Pregnancy—no grace period
  - Restart if > 7 days

Which Partners to Notify?
- Primary: all partners in last 3 months
- Secondary: all partners in last 6 months
- Early latent: all partners in last year
- Late latent: long-term partners

Syphilis is the most contagious within the first year.
“When can I have sex again?”

A) 1 week
B) 2 weeks
C) 1 week if early syphilis, 3 weeks if late latent
D) 3 weeks if early syphilis, 1 week if late latent

“When can I have sex again?”

A) 1 week,
or
After chancre is healed, whichever comes later

Recommend retesting

<table>
<thead>
<tr>
<th></th>
<th>HIV negative</th>
<th>HIV positive</th>
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<tbody>
<tr>
<td>Primary</td>
<td>6, 12 months</td>
<td>3, 6, 9, 12, 24 months</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early latent</td>
<td>6, 12, 24 months</td>
<td>6, 12, 18, 24 months</td>
</tr>
<tr>
<td>Late latency</td>
<td></td>
<td></td>
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</tbody>
</table>

- Adolescents and adults should have 4-fold drop at 12 months
- Reproductive age women who had partial treatment and 4-fold drop still need re-treatment

Clinical Presentation, Diagnosis and Treatment in Neonates and Infants

When During Pregnancy

- Mothers with secondary syphilis
- Transplacental transmission to the fetus
- Transmission occur at any stage of pregnancy

Congenital Syphilis

- Early Disease
  - Manifestations < 2 yrs of age
- Late Disease
  - Symptoms beyond >2 yrs of age
Early Congenital Syphilis
- 30-40% of fetuses are stillborn
- 75% of live born have no symptoms at birth
- Most children demonstrate symptoms b/t 3rd - 14th weeks after birth

Early Congenital Syphilis
- Non-Immune Hydrops
- Preterm Infant
- Intrauterine Growth Restriction
- Hepatomegaly +/- splenomegaly
  - Hepatomegaly most consistent feature

Early Congenital Syphilis
- Dermatologic Findings
  - Rash (vary in appearance)
    - sometimes described as blueberry muffin
  - Pemphigus syphiliticus
    - Vesiculobullosus eruptions on palms/soles
  - Maculopapular rash
    - Starts pink and oval macules, become copper and desquamate

Early Congenital Syphilis
- Hematologic Findings
  - Coombs + hemolytic anemia
  - Thrombocytopenia
  - Leukopenia/leukocytosis

Early Congenital Syphilis
- Mucocutaneous
  - Syphilitic rhinitis “snuffles”
  - Condyloma Lata
    - Mucosal surfaces

Early Congenital Syphilis
- Musculoskeletal
  - Periostitis
  - Wimberger Sign = demineralization of upper tibia
  - Wegeners Sign = “sawtooth metaphysis”
- Pseudoparalysis of Parrot
  - Later Finding
  - Lack of extremity movement due to bone pain
Early Congenital Syphilis

- Neurological
  - Acute syphilitic leptomenigitis
    - Similar presentation to bacterial meningitis
    - CSF findings more c/w septic meningitis (mononuclear predominance)
  - Chronic meningovascular syphilis
    - Onset ~ 1 year
    - Hydrocephalus
    - CN palsy
    - Intellectual/neurodevelopment deterioration

- Other Findings
  - Nephrotic Syndrome
    - Typically can occur 2 – 3 months of age
    - Edema: pretibial, scrotal, periorbital edema, ascitis
  - Jaundice

- Other Findings
  - Nephrotic Syndrome
  - Typically can occur 2 – 3 months of age
  - Edema: pretibial, scrotal, periorbital edema, ascitis

Late Congenital Syphilis

- Hutchinson’s teeth
- Mulberry molars
- Saddle nose deformity
- Various eye findings
- CNS
- Neurosyphilis
- Saber shins
- Higoumenakia sign
- Clutton joints

Neurodevelopmental Outcome

- Verghese, et al, 2018
- 39 births to women with reactive serologies
  - 30 survivors
  - 11 w/ and 7 w/o congenital syphilis w/ ND assessment
- ND impairment documented
  - 3/11 w/ CS & 1/7 w/o CS
- Speech delay occurred in 4/11 CS and 3/7 w/o CS

Diagnosis of Congenital Syphilis

- Fourfold or > maternal nontreponemal Ab titer
- Clinical signs or symptoms
- Missing/undocumented maternal treatment
- Mother treatment <4 wks before delivery
- Mother treatment w/ anything but penicillin
- Maternal evidence of reinfection
Proven or Highly Probable Diagnosis

- Neonate
  - Exam c/w disease
  - Titer fourfold > mother’s*
  - Positive darkfield or PCR of lesions/body fluid

- Evaluation
  - CSF for VDRL, cell count, protein
  - CBC w/ MD
  - Long bone films, CXR, LFTs, BMP, Neuroimaging, Optho exam, Auditory Brain Stem Response

- Treatment
  - Aqueous crystalline Pen G 50,000 units/kg IV q12 during 1st 7 days of life, then IV q8 for 10 days total
  - Procaine Pen G 50,000 units/kg/dose IM daily x 10 days

Possible Congenital Syphilis

- Neonate with mother’s following history
  - Mom not treated/inadequately treated/no documentation
  - Mother treated w/ nonpenicillin G regimen
  - Mother w/ treatments < 4 weeks before delivery

- Evaluation
  - CSF for VDRL, cell count, protein
  - CBC w/ MD
  - Long bone films

- Treatment
  - Aqueous crystalline Pen G 50,000 units/kg IV q12 during 1st 7 days of life, then IV q8 for 10 days total
  - Procaine Pen G 50,000 units/kg/dose IM daily x 10 days
  - Benzathine Pen G 50,000 units/kg/dose IM in a single dose*

Congenital Syphilis Less Likely

- Neonate
  - Normal PE & titers =/< fourfold of mother’s titer…. and
  - Mother adequately treated >4 wks before delivery, and
  - Mother w/ no evidence of relapse

- Evaluation
  - None

- Treatment
  - Benzathine Pen G 50,000 units/kg/dose IM in a single dose*

Congenital Syphilis Unlikely

- Normal PE & titers =/< fourfold of mother’s titer…. And
  - Mother’s treatment before pregnancy
  - Mother’s titers remain low and stable before and during pregnancy & delivery (VDRL <1:2, RPR <1:4)

- Evaluation
  - None

- Treatment
  - None*

Syphilis is Preventable
Reasons treatment doesn’t happen

- No prenatal care
- Initial labs negative, no third trimester test
- Initial labs negative, third trimester test late (after 32 weeks)
- Patient only partly treated (didn’t get all 3 doses)
- Neonatal: lack of communication between OB and pediatrician

Change in DSHS definition (2018)

- Now counted as congenital syphilis:
  - Mother had late latent/unknown duration syphilis pre-pregnancy
  - No adequate treatment documented
  - Not re-treated during pregnancy

Key point #1: Treat if mother RPR+

- Even if she was adequately treated during or before pregnancy (“congenital syphilis less likely,” “congenital syphilis unlikely” categories)
  - 50,000 units/kg in a single dose
  - CDC: “This dose can be omitted if infant can be followed up serologically every 2-3 months for 6 months.”
  - If neonatal RPR NR and mother RPR+, retest at 3 months to rule out serologically negative incubating congenital syphilis at the time of birth.

Key point #2: Timing, not titers

- Risk of congenital syphilis depends more on time interval from treatment until delivery, than on a 4-fold decline in maternal titer.
- UT Southwestern chart review from 1984-2011
  - 166 charts with pre- and post-treatment titers
  - 57% Black, 39% Hispanic, 6% white
  - 4% primary syphilis, 23% secondary, 30% early latent
  - Mean gestational age at treatment 29.1 weeks
  - Mean gestational age at delivery 38 weeks
  - 147 infant outcomes; 18% (27) had congenital syphilis

Table 2.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No 4-Fold Decline</th>
<th>4-Fold Decline</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at treatment, wk</td>
<td>36.3±8.6</td>
<td>27.3±4.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gestational age of delivery, wk</td>
<td>38.1±2.6</td>
<td>38.4±2.9</td>
<td>.49</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>18 (22)</td>
<td>9 (14)</td>
<td>.85</td>
</tr>
</tbody>
</table>
Why a 4-fold drop?

- Reverse sequence serology
  - Syphilis diagnosis requires non-treponemal and treponemal tests
  - Non-treponemal: RPR, VDRL
  - Treponemal: TPPA, FTA, MHA-TP, EIA, CIA
  - What follows is an increasingly common scenario in San Antonio...

Case example

- In prenatal care, RPR NR—so no treponemal test done
- At hospital, maternal EIA+, RPR NR
- Tiebreaker TPPA negative → Treat EIA as a false positive
  - No further action
  - If mother at high risk for very early infection (infected within last 3 weeks), could treat mother and infant
- Tiebreaker TPPA positive: differential dx early primary syphilis, prior syphilis adequately treated, untreated latent syphilis, prozone effect
  - Treat mother and infant

Stop congenital syphilis

- 2017 CDC call to action
  - Take a sexual history in adolescents
  - Test all pregnant adolescents for syphilis
  - If positive, treat immediately
  - Report within 1 business day to public health
- 2018 Metro Health advisory

Congenital syphilis case review team

- Chart abstractions and maternal interview summaries in a multidisciplinary group supported by Metro Health and Texas Department of State Health Services
- Free CME
- Pediatricians needed
- Contact Jessica Del Toro, jessica.deltoro2@sanantonio.gov, and Amanda Reich, amanda.reich@dshs.texas.gov
Thank you. Questions?

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