Congenital Syphilis

Chokechai Rongkavilit, M.D.
Medical Director
Pediatric Infectious Diseases
Case

- 3-hour-old infant male 39 weeks gestation born vaginally without complications.

Mother

- 9 weeks pregnancy: RPR = 1:32
- Treated with benzathine penicillin IM x 3 doses
- Follow up RPR 3 and 5 months later = 1:4 and 1:2
- No RPR after that.

Pediatrician decided to test baby and mother at 1 week after birth

- Mother RPR = 1:8. Baby RPR=1:2
Congenital Syphilis (CS) and Rates of Primary and Secondary Syphilis (P&S) Among Women, United States, 2006–2015

![Graph showing CS and P&S rates from 2006 to 2015]
**Congenital Syphilis in Fresno County compared to California, 2011-2016**

*Fresno County 2016 data is preliminary. California 2016 data is not available.*
Congenital Syphilis Incidence Rates in Fresno County compared to California, 2011-2016

*Fresno County 2016 data is preliminary. California 2016 data is not available.
The Health Officer is designating Fresno County as an area with high syphilis morbidity.

With this designation, best practice and guidelines established by CDPH, CDC, and USPSTF dictate screening for syphilis three times during pregnancy. **Screen ALL Fresno County pregnant women at the initial prenatal visit, again EARLY in the third trimester of pregnancy, and again at delivery.**

Prevention of congenital syphilis is an urgent public health matter. Congenital syphilis can be prevented if the mother is diagnosed and treated appropriately and without delay, and the baby is evaluated and treated per CDC STD Treatment Guidelines which can be found at [http://www.cdc.gov/std/treatment/default.htm](http://www.cdc.gov/std/treatment/default.htm)

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Recognize The Symptoms

After 3-8 weeks lesions disappear spontaneously.
4 stages of Syphilis (not congenital)

<table>
<thead>
<tr>
<th>Primary</th>
<th>Chancre (painless, non-itchy ulcer with clean base)</th>
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<tbody>
<tr>
<td>1-4 weeks after exposure</td>
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<tr>
<th>Secondary</th>
<th>Symmetrical non-itchy rash including palms and soles Condyloma lata (flat whitish wart-like lesion) Fever, sore throat, malaise, hair loss 40-85% do not report chancre.</th>
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<tbody>
<tr>
<td>4-10 weeks</td>
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<thead>
<tr>
<th>Latent</th>
<th>Asymptomatic</th>
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<tbody>
<tr>
<td>Early (&lt;1 yr)</td>
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<tr>
<td>Latent-Late (&gt;1 yr)</td>
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<thead>
<tr>
<th>Tertiary</th>
<th>Gummatous form Neurosyphilis: paresis, tabes dorsalis, dementia Cardiovascular form: aortitis, aortic aneurysm</th>
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<tr>
<td>3-15 years</td>
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<td>(30% of infected persons)</td>
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Primary: Chancre

Secondary
CDC Screening Recommendation

- Pregnant women – screened early in pregnancy (first prenatal visit)
- Our region:
  - Initial prenatal visit
  - Two more: at 28-32 weeks gestation and at delivery

Tests:
- Non-treponemal (RPR and VDRL)
- Treponemal (EIA-automated, FTA-ABS, MHA-TP, TP-PA)
Non-treponemal Tests
RPR & VDRL

- Inexpensive, rapidly performed, sensitive, but not specific

- Semiquantitative results (titer); help define disease activity and monitor response to therapy.

- False negative:
  - Early primary syphilis
  - Latent syphilis of long duration
  - prozone phenomenon: high concentrations of antibody

- False-positive:
  - viral infections (EBV, hepatitis, varicella, and measles), lymphoma, tuberculosis, endocarditis, connective tissue disease, pregnancy, IVD use, or Wharton jelly contamination (umbilical cord blood)
Non-treponemal Tests
RPR & VDRL

- Titer decreases 4-fold in 6 to 12 months after therapy.
- Become nonreactive in 1 year after successful therapy.
- **Serofast**: Remain low stable titers (1:4 or lower) despite therapy. More common in patients treated for latent or tertiary syphilis.
- RPR and VDRL are not interchangeable.
Treponemal Tests

TP-EIA/CIA (automated), TP-PA and FTA-ABS

• High specificity → Confirmatory test

• Remain reactive for life, even after successful therapy. Should NOT be used to assess response to therapy.

• 15%-25% of patients treated during the primary stage revert to being serologically nonreactive after 2-3 years.

• False positive: other spirochetal diseases (yaws, pinta, leptospirosis, rat-bite fever, relapsing fever, and Lyme disease).
Treatment of Pregnant Women

- **Primary, secondary or early latent** syphilis
  - Benzathine penicillin 2.4 million units IM in a single dose

- **Late latent** syphilis or **Unknown duration**
  - Benzathine penicillin 2.4 million units for 3 doses IM at 1-week interval

- Women and Sex partners should be treated, followed, and documented for treatment response.
Congenital Syphilis
Congenital Syphilis

Transmission:

- Transplacental
- Direct contact with lesions during birth.
- Treponema pallidum is not transmitted via breast milk, except if mother has a lesion (e.g. chancre) on her breast.
Congenital Syphilis (CS)

- CS is estimated to occur in 25-75% of exposed infants, with mortality rate 1-3%.

Transmission risk from mother to fetus:

- Untreated primary or secondary syphilis
  - 60-100% transmission risk
  - 40% risk of abortion, stillbirth, or perinatal death
  - 41% risk of giving birth to a live but infected infant.

- Untreated late syphilis results in
  - 40% transmission risk in early latent stage and <10% in late latent stage
  - 12% risk of stillbirth
  - 2% risk of giving birth to infected infant

Schmid GP. Sex Transm Dis. 2007;34:S5
AAP Red Book 2015
Clinical Manifestations

Two stages: Early <2yr and Late >2 yr of life.

**Early Manifestations:** asymptomatic (2/3 of cases), or:

- **Gestational/perinatal:** stillbirth, hydrops fetalis, prematurity, LBW, large placenta, necrotizing funisitis.

- **Systemic:** fever, epitrochlear lymph node enlargement, edema, failure to thrive, hepatosplenomegaly.

- **Mucocutaneous:**
  - Rhinitis (snuffles), contains spirochetes (contact precautions)
  - Rash: Maculopapular, Oval lesions, red or pink then turn coppery brown; desquamation particularly on palms or soles, contains spirochetes.
Early Manifestations

- **Hematologic**: Anemia, Thrombocytopenia, Leukopenia

- **Musculoskeletal**: Long-bone abnormalities resulting in characteristic radiological features:
  - Periostitis: Irregular periosteal thickening; usually present at birth.
  - Wegner sign: Metaphyseal serration or "sawtooth metaphysis"
  - Wimberger sign: Osseous destruction of upper medial tibia.
  - “Moth-eaten” appearance
  - Pathologic fractures or pain, which limits movement of extremity, giving the appearance of paralysis ("pseudoparalysis of Parrot")
Early Manifestations

- **Neurologic:**
  - **Acute leptomenigitis:** usually ~ 3-6 mo; presentation similar to bacterial meningitis but CSF findings more consistent with aseptic meningitis (mononuclear predominance); responds to penicillin therapy.
  - **Chronic meningovascular syphilis:** ~ the end of the first year; hydrocephalus; cranial nerve palsies; neurodevelopmental deterioration; cerebral infarction.

- **Others:** Pneumonia/pneumonitis, Nephrotic Syndrome.
Early Manifestations
Early Manifestations
Early Manifestations

- Periostitis
- Wimberger Sign
- Diaphyseal destruction
Late Manifestations

- >2 yrs of life, result of scarring or persistent inflammation from early infection characterized by gumma formation.
- **Facial**: Frontal bossing, saddle nose, short maxilla, protuberant mandible
- **Ears**: Sensorineural hearing loss
Late Manifestations

- Hutchinson teeth
- Mulberry molars
- Interstitial keratitis, chorioretinitis, glaucoma, corneal scar, optic atrophy
- Perforation of hard palate
Late Manifestations

- **Cutaneous:** Gummas and Rhagades (perioral fissures or a cluster of scars radiating around the mouth).

- **CNS:** Intellectual disability, arrested hydrocephalus, cranial nerve palsies.

- **Skeletal:**
  - Saber shins (anterior bowing of the tibia)
  - Clutton joints (painless arthritis)
**CONCERNING INCREASES IN SYPHILIS IN WOMEN AND CONGENITAL SYPHILIS:**

**AN UPDATE FOR CALIFORNIA HEALTH CARE PROVIDERS**

**Prenatal Screening: It’s the Law!**

All pregnant women should receive routine prenatal care which includes syphilis testing. **In California, it is required by law that pregnant women get tested for syphilis at their first prenatal visit.**

Syphilis testing should be repeated during the third trimester (28-32 weeks gestational age) and at delivery in women who are at high risk for syphilis or live in areas with high rates of syphilis, particularly among females. Routine risk assessment should be conducted throughout pregnancy to assess the risk factors highlighted in the box on page 2; this should inform the need for additional testing.

**Infants should not be discharged from the hospital unless the syphilis serologic status of the mother has been determined at least once during pregnancy and, for at-risk women, again at delivery.**

Maternal evaluation should include the following:

- The mother’s syphilis serology before/throughout pregnancy
- Adequacy of maternal treatment

### Inadequate therapy
- Treatment with a nonpenicillin antibiotic
- Treatment less than four weeks before delivery (including treatment with penicillin)
- Inappropriate dose for stage of disease

### Inadequate documentation of maternal treatment
- Lack of performance of serial non-treponemal* antibody titers after maternal treatment
- Maternal therapy was not documented

### Inadequate response to therapy
- Maternal non-treponemal antibody titers did not decline at least fourfold (two dilutions) after treatment
- Maternal non-treponemal antibody titers suggest reinfection or relapse (ie, fourfold increase)
Infant Evaluation

- Physical examination
- Darkfield microscopic exam or DFA staining of suspicious lesions or body fluids (e.g. nasal discharge)
- Serum RPR (not cord blood)
- CSF analysis for VDRL, cell count, and protein
- CBC with differential and platelet count
- Pathologic examination of the placenta or umbilical cord with fluorescent antitreponemal antibody staining
- Other tests as clinically indicated (chest radiograph, long-bone radiographs, liver function tests, abdominal ultrasound, ophthalmologic examination, auditory brain stem response, and neuroimaging studies)
- Although CSF results do not alter the treatment, it is necessary to determine the need for subsequent monitoring.
Diagnosis of Congenital Syphilis

- confirmation of maternal syphilis
- adequacy of maternal therapy (PCN 4 wk before delivery)
- maternal response to therapy (4-fold decrease in RPR)
- comparison of maternal and infant RPR at delivery
- evaluation of infant's nontreponemal serology, physical examination, and laboratory tests (liver function tests; CBC; and CSF cell count, protein, and quantitative VDRL)

AAP Red Book 2015
Reactive maternal RPR/VDRL

Nonreactive maternal treponemal test*

- False-positive reaction: no further evaluation

Reactive maternal treponemal test**

- Maternal treatment:
  - None, OR
  - Undocumented, OR
  - 4 wk or less before delivery, OR
  - Nonpenicillin drug, OR
  - Maternal evidence of reinfection/relapse (fourfold or greater increase in maternal titers)$^\Delta$

- Maternal penicillin treatment during pregnancy AND more than 4 weeks before delivery, AND no evidence of maternal reinfection or relapse

Adequate maternal treatment before pregnancy with stable low titer (serofast),$^\Diamond$ AND infant examination normal; if infant examination is abnormal, proceed with evaluation$^5$

- No evaluation
- No treatment$^\Xi$

Evaluate$^5$

- Infant physical examination normal; evaluation normal; infant RPR/VDRL same or less than fourfold the maternal RPR/VDRL titer$^\Delta$
  - Treatment$^+$

- Infant physical examination abnormal; OR evaluation abnormal or incomplete; OR RPR/VDRL at least fourfold greater than maternal RPR/VDRL titer$^\Delta$
  - Treatment (Option 1)

Infant RPR/VDRL fourfold or greater than maternal RPR/VDRL titer$^\Delta$

- Infant physical examination abnormal

Infant RPR/VDRL same or less than fourfold the maternal RPR/VDRL titer$^\Delta$

- Infant physical examination normal

Evaluation$^5$ and Treatment (Option 1)

No evaluation; Treatment (Option 2)

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TREATMENT OPTIONS:

1. Aqueous penicillin G, 50,000 U/kg, intravenously, every 12 hours (1 week of age or younger) or every 8 hours (older than 1 week); or procaine penicillin G, 50,000 U/kg, intramuscularly, as a single daily dose for 10 days. If 24 or more hours of therapy is missed, the entire course must be restarted.

2. Benzathine penicillin G, 50,000 U/kg, intramuscularly, single dose.
Maternal treatment:
None
Undocumented
4 wk or less before delivery
Non-penicillin
Reinfection/Relapse/RPR<4 folds drop

Infant evaluation:
Serology: RPR
CBC
CSF, with VDRL
AST/ALT*
Long bone radiograph*
Eye/Hearing exam*
Neuroimaging*

Infant with normal exam, normal evaluation, and RPR same or <4 folds of maternal titer
1) Treat PCN 10 days
2) Single benz PCN if F/U is certain

Infant with abnormal exam, abnormal evaluation, or RPR ≥ 4 folds of maternal titer
Treat PCN 10 days
Mother treatment with PCN >4 wk before delivery AND no evidence of reinfection/relapse

- Infant RPR ≥4 folds of mother RPR
  - Infant evaluation AND PCN IV 10 days

- Infant RPR <4 folds of mother RPR
  - Infant physical exam abnormal
    - Infant evaluation AND PCN IV 10 days
  - Infant physical exam normal
    - No evaluation Benz PCN 1 dose IM
Mother in serofast (RPR 1:4 or less for over 1 yr after successful treatment

- Infant physical exam abnormal
  - Infant evaluation
- Infant physical exam normal
  - No evaluation and no treatment
  - Benz PCN 1 dose if F/U uncertain
Treatment of Congenital Syphilis

- Parenteral **penicillin** is the drug of choice

- **Ten Day Regimen:** Two options:
  - Aqueous penicillin G 50,000 units/kg **IV** every 12 hours (for infants ≤7 days of age) and every 8 hours (for infants >7 days of age) for a total of 10 days.
  - Procaine penicillin G 50,000 units/kg **IM** as a single daily dose for 10 days.

- **Single Dose Regimen:**
  - Benzathine penicillin G (50,000 units/kg) **IM** as a single dose
Follow-Up

• Nontreponemal tests every 2 to 3 months until nonreactive or the titer has decreased at least 4 folds.

• Nontreponemal titers should decrease by 3 months of age and should be nonreactive by 6 months of age.

• Infants with positive CSF VDRL or abnormal CSF cell counts and/or protein should undergo CSF examination at 6-month intervals until CSF is normal.

• A reactive serum RPR or CSF VDRL at 6-month interval is an indication for retreatment.
Recommended Reading

CDC website on STD Treatment Guidelines 2015