Update on Syphilis in Women and Congenital Syphilis

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Overview

• Review the epidemiology of syphilis in women and congenital syphilis in California
• Describe clinical manifestations, screening recommendations, diagnostic approach, staging, and treatment of syphilis in women
• Describe characteristics of congenital syphilis cases in California
• Identify key resources for questions about the management of syphilis among pregnant women and infants
Chlamydia, Gonorrhea, and Early Syphilis

- **Chlamydia**: 504.4 (N=198,503)
- **Gonorrhea**: 164.3 (N=64,677)
- **Early Syphilis**: 28.5 (N=11,222)

Rate per 100,000 population

Year

Early Syphilis*, Number of Cases by Gender & Gender of Sex Partners, California, 1996–2016

* Includes primary, secondary, and early latent syphilis.
Female Early Syphilis* Cases
California, 2009–2016

* Includes primary, secondary, and early latent syphilis.
Early Syphilis*
Incidence Rates by Gender and Age Group (in years)
California, 2016

* Includes primary, secondary, and early latent syphilis.
Early Syphilis*, Incidence Rates by County and Gender
California, 2016

* Includes primary, secondary, and early latent syphilis.
Early Syphilis*
Incidence Rates for Females by Race/Ethnicity
California, 2007–2016

* Includes primary, secondary, and early latent syphilis.

Note: NA/AN = Native American/Alaskan Native, A/PI = Asian/Pacific Islander.
Race/ethnicity “Not Specified” ranged from 0% to 6.7% of cases for females in any given year.

MSM=Men who have sex w/men, MSW=Men who have sex w/women, MSM&W=Men who have sex with men & women

* Includes primary, secondary, and early latent syphilis.

Note: The Modified Kaufman Criteria were used through 1989. The CDC Case Definition (MMWR 1989; 48: 828) was used effective January 1, 1990. California data prior to 1985 include all cases of congenital syphilis, regardless of age.
## Congenital Syphilis — States With Highest Number of Cases and Highest Rates per 100,000 Live Births, 2016

<table>
<thead>
<tr>
<th>States with Highest Number of Cases:</th>
<th>States with Highest Rates:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rank</strong></td>
<td><strong>State</strong></td>
</tr>
<tr>
<td>1</td>
<td>California</td>
</tr>
<tr>
<td>2</td>
<td>Texas</td>
</tr>
<tr>
<td>3</td>
<td>Florida</td>
</tr>
<tr>
<td>4</td>
<td>Louisiana</td>
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<td>5</td>
<td>Georgia</td>
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<td>6</td>
<td>Illinois</td>
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<td>7</td>
<td>North Carolina</td>
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<td>8</td>
<td>Maryland</td>
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<td>9</td>
<td>Arizona</td>
</tr>
<tr>
<td>10</td>
<td>New York</td>
</tr>
<tr>
<td>10</td>
<td>Michigan</td>
</tr>
</tbody>
</table>

California congenital syphilis cases represented 33% of all CS cases in the U.S. in 2016.
Congenital Syphilis Cases versus Female Early Syphilis* Incidence Rates, California, 2008–2017**

* Includes primary, secondary, and early latent syphilis.
** Provisional data; not for distribution.
Syphilis 101

- Causative organism: *Treponema pallidum*, a spirochete bacterium
- Transmission:
  - Sexual (intimate skin-to-skin contact)
  - Vertical
  - Blood
- Causes systemic infection
- Characterized by episodes of active disease during which patients have signs/symptoms of infection, interrupted by periods of latent infection
  - Lab testing is required to diagnose patients
- Incubation period: 10-90 days

Image courtesy: Gregory Melcher, UC Davis
Susan Philip, SF DPH & UCSF
Prevention of congenital syphilis requires prevention/treatment of maternal syphilis
Syphilis Natural History

- **Exposure**: 30-50%
  - Incubation Period: 3-4 weeks

- **Primary**: 2-6 weeks

- **Secondary**:
  - 25%
  - Possible relapse
  - After 3-8 weeks lesions disappear spontaneously

- **Latent**: 30%
  - 2-20 years

- **Tertiary**

**Neurosyphilis can occur at any stage**
Primary Syphilis

– Chancre (ulcer) appears 10-90 days after infection
  • Single, painless, indurated, clean-based lesion with rolled edges (textbook chancre)
  • More likely to be multiple lesions and persisting at the time of secondary syphilis in HIV-infected patients
  • Can go unrecognized
– Can have regional adenopathy (rubbery, bilateral, painless)
Secondary Syphilis

- Usually occurs 3-6 weeks after primary chancre
  - Rash (75-90%), involving palms/soles (60%)
  - Generalized lymphadenopathy (70-90%)
  - Constitutional symptoms (50-80%)
  - Mucous patches (5-30%)
  - Condyloma lata (5-25%)
  - Patchy alopecia (10-15%)
  - Symptoms of neurosyphilis (1-2%)
  - Less common: meningitis, hepatitis, arthritis, nephritis

Courtesy: Gregory Melcher, UC Davis
Susan Philip, SF DPH & UCSF
Latent Syphilis

- No symptoms
- Relapse possible in early latent
- Important to treat to:
  - Prevent complications
  - Prevent transmission from pregnant woman to fetus
Tertiary Syphilis

• Gummas (liver, bone, others)
• Cardiovascular (including aortitis)
• Tabes dorsalis
• General paresis

Source: CDC/NCHSTP/Division of STD prevention, STD Clinical Slides
Neurosyphilis: Can Occur at Any Stage of Syphilis

- All patients with syphilis should be evaluated for neurologic symptoms and signs
- Asymptomatic CNS invasion is common in early syphilis
  - Clinical significance of abnormal CSF findings in asymptomatic early syphilis is unclear
- Neurosyphilis
  - Early manifestations (months to years after infection)
    - Cranial nerve dysfunction, meningitis, stroke, altered mental status, hearing or vision changes
  - Late manifestations (10-30 years after infection)
    - Tabes dorsalis and general paresis
- Ocular syphilis and otosyphilis
Syphilis Staging Flowchart

**SIGNS OR SYMPTOMS?**

- **YES**
  - Chancre
  - Rash, etc.

  **PRIMARY**

- **YES**
  - Rash, etc.

  **SECONDARY**

- **NO**

  **LATENT**

  **ANY IN PAST YEAR?**
  
  - Negative syphilis serology
  - Known contact to an early case
  - Good history of typical signs/symptoms
  - 4-fold increase in titer
  - Only possible exposure was this year

  **EARLY LATENT (< 1 year)**

- **NO**

  **LATE LATENT or UNKNOWN DURATION**
Treatment is Based on Duration of Infection

**In pregnancy, should adhere to 7 days between doses

*Bicillin L-A is the trade name. DO NOT USE Bicillin C-R!*

Benzathine penicillin G 2.4 million units IM in a single dose

Benzathine Penicillin G 2.4 million units once per week for 3 weeks**

CDC 2015 STD Treatment Guidelines
www.cdc.gov/std/treatment
Syphilis Treatment Alternatives for Penicillin Allergic Non-Pregnant Adults

Primary, Secondary, & Early Latent
- Doxycycline 100 mg po bid x 2 weeks
- Tetracycline 500 mg po qid x 2 weeks
- Ceftriaxone 1 g IV (or IM) qd x 10-14 d
- Azithromycin 2 g po in a single dose*

Late Latent
- Doxycycline 100 mg po bid x 4 weeks
- Tetracycline 500 mg po qid x 4 weeks

In pregnancy, benzathine penicillin is the only recommended therapy. No alternatives.

* Do NOT use azithromycin in MSM or pregnant women
Who Should be Screened for Syphilis?

- Pregnant women at first prenatal visit
  - And again in the third trimester and at delivery (if at high risk, or residing in area with high syphilis morbidity)

- MSM, including those on PrEP
  - Annually, or more frequently, 3-6 months if at high risk (multiple, anonymous partners, meth use)

- Correctional settings
  - Universal screening based on local area or institutional incidence

- HIV-infected individuals (at least annually)

- STD clinics / Clients with other STDs
Diagnosing Syphilis

• Syphilis is diagnosed by:
  – Reviewing patient history
  – Assessing sexual risk
  – Conducting a physical exam
  – Interpreting serologic test results
Syphilis Screening Paradigm

**REVERSE SEQUENCE**

**Treponemal tests (e.g., EIA, CIA, MBIA)**
- **TP-SPECIFIC ANTIBODIES**
- QUALITATIVE
- USUALLY DETECTABLE FOR LIFE
  - REACTIVITY DECLINES WITH TIME

**Non-treponemal tests (e.g., RPR, VDRL)**
- **NON-SPECIFIC ANTIBODIES TO LIPOIDAL ANTIGENS**
  - QUANTITATIVE
  - REACTIVITY DECLINES WITH TIME

*Reflex to*

Need both types of serologic tests to make syphilis diagnosis; Use of only one type of test is insufficient.
Syphilis serologic screening algorithms

**Traditional**

- Quantitative RPR
  - RPR+
    - TP-PA or other trep. test
      - TP-PA+ Syphilis (past or present)
      - TP-PA- Syphilis unlikely
  - RPR-

**Reverse sequence**

- EIA or CIA
  - EIA/CIA+
    - Quantitative RPR
      - RPR+
        - Syphilis (past or present)
      - RPR-
        - TP-PA
          - TP-PA+ Syphilis (past or present)
          - TP-PA- Syphilis unlikely
Diagnostic Challenges

False negatives

- Early primary and late latent stages
  - Serology may be negative in up to 25% of primary syphilis cases
- Prozone reaction (RPR/VDRL)

Biologic False Positives

- Non-trep test positive with confirmatory Treponemal test negative
- Viral illnesses including HIV, recent immunizations, autoimmune and chronic diseases

Discordant serology

- EIA or CIA + and RPR –

Geisler MG. *South Med Jour* 2004, **97**: 327-328.
Use of Treponemal Immunoassays for Screening and Diagnosis of Syphilis

Guidance for Medical Providers and Laboratories in California

February 2016

CDPH has materials available online: std.ca.gov
Brief Clinical Overview of Congenital Syphilis
Early Congenital Syphilis (<age 2)
Common Presentations and Physical Findings

- Asymptomatic presentations are common
  - ~2/3 infants born with CS are asymptomatic at birth – if untreated will develop symptoms
- Bone abnormalities
- Enlargement of liver +/- jaundice
  - Hepatomegaly present in almost all infants with CS
- Skin rash
- Nasal discharge ("snuffles")
- Blood abnormalities
- Neurologic abnormalities
- Others
Early

Snuffles

Cutaneous lesion

Mucous patches

Pneumonia Alba

Syphilitic rash

Courtesy CDC Public Health Image Library
Late Congenital Syphilis (>age 2)  
Physical Findings

- Hearing loss (puberty – adulthood).
  - Can develop suddenly
- Interstitial keratitis (5 years old – adulthood)
  - Inflammation of tissue of cornea, can lead to vision loss
- Bone or tooth abnormalities
- Neurologic abnormalities
- Gummas (granulomatous inflammatory response to spirochetes) in the skin or mucous membranes
- Others
Interstitial Keratitis

Photos courtesy of Public Health Image Library, CDC/Susan Lindsley
Hutchinson’s Teeth

Permanent incisor teeth are narrow and notched.

Photos courtesy of Public Health Image Library, CDC/Susan Lindsley (left) and Robert Sumpter (rt).
Perforation of hard palate
Clutton’s Joints

Saber Shins

Photos courtesy of Public Health Image Library, CDC/J. Pledger
Syphilis in Pregnancy and Congenital Syphilis
Screening Recommendations – CDC

• All pregnant women should be screened for syphilis at the first prenatal visit
• Women who are at high risk for syphilis, live in areas of high syphilis morbidity, or are previously untested should be screened again both:
  – Early in the third trimester (approx 28 weeks GA)
  – At delivery

Penicillin treatment of pregnant women with syphilis is highly effective at preventing CS
Women who would benefit from additional syphilis testing in the 3rd trimester and at delivery include those who:

- Have signs and symptoms of syphilis infection
- Live in areas with high rates of syphilis, particularly among females
- Were diagnosed with an STD during pregnancy
- Receive late or limited prenatal care
- Have partners that may have other partners, or partners with male partners
- Have history of incarceration
- Are involved with substance use or exchange sex for money, housing, or other resources

Routine risk assessment should be conducted throughout pregnancy to assess risk factors and inform the need for additional testing.

California Counties with Third Trimester +/- Delivery Syphilis Screening Recommendations for All Pregnant Women, 6/2017

Early Syphilis* among Females of Childbearing Age (15-44) Incidence Rates by County, California, 2016

* Includes primary, secondary, and early latent syphilis.

Rate per 100,000:
- 0 cases reported
- < 2
- 2 to 3.9
- 4 to 9.9
- 10 +
CDC Screening Recommendations

- No infant should leave the hospital without the maternal serologic status having been determined at least once during pregnancy, and again at delivery if at risk.
  - If mother presents at delivery with no prenatal care, STAT RPR should be performed
  - If baby has congenital syphilis and is asymptomatic, there is still an opportunity to treat the infant to prevent further morbidity
- Any woman who delivers a stillborn infant should be tested for syphilis
Treatment of Syphilis in Pregnancy

• The only treatment of syphilis in pregnancy is penicillin. There are no alternatives.
• Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection.
  – Some experts recommend a 2nd dose of benzathine penicillin G be given a week after the initial dose in early syphilis
• Pregnant women with penicillin allergy should be desensitized and treated with penicillin.

All patients with syphilis should be tested for HIV.
Highest risk of treatment failure occurs during early syphilis

Table 3. Success of Maternal Treatment to Prevent Congenital Syphilis by Stage of Infection

<table>
<thead>
<tr>
<th>Stage</th>
<th>Success/Total treated</th>
<th>Percentage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>27/27</td>
<td>100 (87.2, 100)</td>
</tr>
<tr>
<td>Secondary</td>
<td>71/75*</td>
<td>94.7 (86.9, 98.5)</td>
</tr>
<tr>
<td>Early latent</td>
<td>100/102</td>
<td>98 (93.1, 99.8)</td>
</tr>
<tr>
<td>Late latent</td>
<td>136/136</td>
<td>100 (97.3, 100)</td>
</tr>
<tr>
<td>Total</td>
<td>334/340</td>
<td>98.2 (96.2, 99.3)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
* P = .03 compared with other groups, χ².

Overall, maternal treatment is highly effective in the prevention of CS

Maternal treatment more likely to be successful when administered at earlier gestational age

Table 4. Success of Maternal Treatment in Preventing Congenital Syphilis by Gestational Age

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Success/Total treated</th>
<th>Percentage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤20 wk</td>
<td>152/153</td>
<td>99.4 (96.4, 100)</td>
</tr>
<tr>
<td>21–25 wk</td>
<td>51/51</td>
<td>100 (93.0, 100)</td>
</tr>
<tr>
<td>26–30 wk</td>
<td>58/59</td>
<td>98.3 (90.9, 100)</td>
</tr>
<tr>
<td>31–35 wk</td>
<td>44/46</td>
<td>95.6 (85.2, 99.5)</td>
</tr>
<tr>
<td>36–40 wk</td>
<td>26/28</td>
<td>92.9 (76.5, 99.1)</td>
</tr>
<tr>
<td>41–42 wk</td>
<td>3/3</td>
<td>100 (29.2, 100)</td>
</tr>
<tr>
<td>Total</td>
<td>334/340</td>
<td>98.2 (96.2, 99.3)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
P = not significant, $\chi^2$.

Syphilis in Pregnancy: Management

• When syphilis is diagnosed during the second half of pregnancy, management should include an obstetric ultrasound
  • If hepatomegaly, ascites, hydrops, fetal anemia, or thickened placenta- greater risk of fetal treatment failure

• Women treated during second half of pregnancy are at risk for premature labor and/or fetal distress as part of Jarisch-Herxheimer reaction
  • Counsel to seek medical attention if symptoms
  • Concern for this complication should not delay treatment
Syphilis in Pregnancy: Follow-up

- Titers at 28-32 weeks of gestation, delivery, and following recommendations for stage of disease
- Serologic titers can be checked monthly in high-risk women
- Clinical and serologic response should be appropriate for stage
  - Most women will deliver before serologic response to treatment can be assessed
What are common pathways that a women delivers a baby with CS?

**Woman acquires syphilis prior to pregnancy**
- Not diagnosed, not tested
- Not adequately treated
- **SHE BECOMES PREGNANT**

**She acquires syphilis during pregnancy**
- Not diagnosed
  - (late to prenatal care or no prenatal care, early screen negative and not repeated, seroconverted after birth)
- Not treated
  - (treatment not ordered, lost to follow up)
- Late to treatment
  - (treatment initiated <30 days prior to delivery)
- Inadequate treatment
  - (wrong drug or dose, lack or delay in 2nd or 3rd shots for late latent syphilis)

RARELY, among those diagnosed and treated:
- Maternal treatment failure
- Fetal demise
- Permanent fetal damage prior to treatment
What do we know about the cases?
California Project Area CS Cases 2007-2015:
Infant Characteristics (n=391)

- Stillbirth: 7%
- Signs of CS on exam: 11%
- Long bone abnormalities: 10%
- Reactive CSF VDRL: 9%
- Abnormal CSF: 32%
- Preterm birth: 30%

Credits: Stoltey, Ng
Number of congenital syphilis cases, by maternal stage: Majority of mothers had late syphilis

<table>
<thead>
<tr>
<th>Year</th>
<th># of congenital syphilis cases</th>
<th>Late syphilis</th>
<th>Early syphilis</th>
<th>Unknown stage</th>
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<tbody>
<tr>
<td>2007</td>
<td>(n=36) 36 cases</td>
<td>61%</td>
<td>42%</td>
<td>5%</td>
</tr>
<tr>
<td>2008</td>
<td>(n=26) 26 cases</td>
<td>61%</td>
<td>42%</td>
<td>7%</td>
</tr>
<tr>
<td>2009</td>
<td>(n=28) 28 cases</td>
<td>61%</td>
<td>42%</td>
<td>7%</td>
</tr>
<tr>
<td>2010</td>
<td>(n=20) 20 cases</td>
<td>50%</td>
<td>50%</td>
<td>0%</td>
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<tr>
<td>2011</td>
<td>(n=18) 18 cases</td>
<td>56%</td>
<td>44%</td>
<td>0%</td>
</tr>
<tr>
<td>2012</td>
<td>(n=23) 23 cases</td>
<td>61%</td>
<td>39%</td>
<td>0%</td>
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<tr>
<td>2013</td>
<td>(n=50) 50 cases</td>
<td>62%</td>
<td>38%</td>
<td>0%</td>
</tr>
<tr>
<td>2014</td>
<td>(n=70) 70 cases</td>
<td>65%</td>
<td>35%</td>
<td>0%</td>
</tr>
<tr>
<td>2015</td>
<td>(n=120) 120 cases</td>
<td>63%</td>
<td>37%</td>
<td>0%</td>
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</tbody>
</table>

Credits: Stoltey, Ng
STD Control Branch
Percent of congenital syphilis cases, by maternal age at delivery: Majority of mothers were ages 20-29

<table>
<thead>
<tr>
<th>Age</th>
<th>% of cases</th>
<th>Count</th>
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<tbody>
<tr>
<td>&lt; 20</td>
<td>8%</td>
<td>32</td>
</tr>
<tr>
<td>20-29</td>
<td>58%</td>
<td>227</td>
</tr>
<tr>
<td>30-39</td>
<td>32%</td>
<td>123</td>
</tr>
<tr>
<td>40-44</td>
<td>1.5%</td>
<td>6</td>
</tr>
<tr>
<td>45-49</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>50+</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>
Congenital Syphilis
Incidence Rates per 100,000 (L) and Number of Cases (R) by Race/Ethnicity of Mother, California, 2016

Incidence Rates

Number of Cases
When did mother initiate prenatal care? 

Over half of mothers initiated prenatal care only in 3rd trimester or not at all.

- 1st trimester (n=75, 19.2%)
- 2nd trimester (n=57, 14.6%)
- 3rd trimester (n=63, 16.1%)
- No prenatal care (n=137, 35.0%)
- Unknown (n=14, 3.6%)
- Received prenatal care, outside CA (n=3, 0.8%)
- Received prenatal care, missing info (n=42, 10.7%)

Nationally, 74% initiate in 1st Trimester; only 6% in 3rd Trimester or not at all (CDC, 2011)
Syphilis screening at first prenatal care visit

Among 199 mothers with documented first prenatal visit:

Possible reasons for delay:
- Provider error
- Lab off-site
- Patient lost to follow-up and labs never drawn
- Surveillance data incomplete

Tested within 7 days of first visit, n=119, 60%
Delayed or not tested, n=80, 40%

Credits: Stoltey, Ng
STD Control Branch

[CDPH Public Health Logo]
Maternal risk characteristics for interviewed early syphilis cases (n=92)

70% (92 of 132) interviewed

- Methamphetamine use
  - 2007-12 (n=46): 22% (n=10)
  - 2013-15 (n=46): 44% (n=20)

- Exchange of sex for money, drugs
  - 2007-12 (n=46): 6.5% (n=3)
  - 2013-15 (n=46): 13% (n=6)

- Jail, juvenile hall, prison
  - 2007-12 (n=46): 13% (n=6)
  - 2013-15 (n=46): 13% (n=6)

Risk in 12 months prior to diagnosis
Public Health Response:
Points of Intervention to Prevent CS

**Pre-pregnancy**
- Screening/dx/tx
- Timely partner services
- Accessible highly effective contraception

**During pregnancy**
- Linkage to prenatal care
- Screening/dx
- **Timely** treatment appropriate for stage
- **Timely** partner services
- Case management
- Prevent and detect new infection

**Birth**
- Evaluation and treatment of baby
Evaluation of Infants Born to Mothers with Syphilis

• CDC STD Treatment Guidelines have detailed guidance on evaluation and treatment
• Treatment decisions based on:
  – Identification of syphilis in the mother
  – Adequate maternal treatment
  – Clinical, lab, x-ray evidence of syphilis in neonate
  – Comparison of maternal (at delivery) and neonatal **nontreponemal** titers (same test-preferably same lab)

Maternal non-trep and trep IgG antibodies can transfer via placenta thus complicating interpretation of neonate serologies
Evaluation of Infants (during first month of life) Born to Mothers with Syphilis

- All infants born to women with reactive syphilis serology should be evaluated with a quantitative nontreponemal test (do not use cord blood, which may be contaminated by mother’s blood)
- Thorough physical exam for evidence of congenital syphilis
- Darkfield exam or PCR testing of suspicious lesions or body fluids (e.g., nasal discharge) and placenta
Scenario 1: ”Proven or Highly Probable Congenital Syphilis”

- Abnormal physical exam consistent with congenital syphilis
  OR
- Serum VDRL/RPR titer that is 4-fold higher than maternal titer
  OR
- Positive darkfield or PCR of lesions or body fluids (or placenta)

➢ Full work-up and 10 days treatment recommended
“Full” Evaluation for Congenital Syphilis

- Careful physical exam
- CSF analysis for VDRL, cell count and protein
- CBC with differential
- Other tests as indicated, including:
  - X-rays (long bone and chest)
  - Liver function tests
  - Ophthalmologic exam
  - Neuroimaging
  - Auditory brainstem response
Scenario 2: “Possible Congenital Syphilis”

Normal physical exam, Nontrep Titer = or < 4-Fold Maternal Titer
AND

Maternal factors:
- Not treated, inadequately treated, or no documentation of treatment OR
- Treatment with erythromycin or other nonstandard regimen OR
- Maternal treatment less than 4 weeks prior to delivery

➢ Work-up/Rx:
- Complete evaluation if 10 days treatment not planned
- Complete evaluation not necessary if 10 days treatment given
- If complete evaluation is normal and infant follow-up certain, single dose benzathine PCN, 50,000 U/KG IM may be given
Scenario 3: “Congenital Syphilis Less Likely”

Normal physical exam, Nontrep Titer = or < 4-Fold Maternal Titer

AND

Maternal factors:

▪ Treated during pregnancy, treatment was appropriate and administered > 4 weeks prior to delivery  AND

▪ No evidence of reinfection or relapse

➢ Work-up/Rx:

▪ No evaluation needed, but **single dose benzathine PCN 50,000 U/KG IM recommended**
Scenario 4: “Congenital Syphilis Unlikely”

Normal physical exam, Nontrep Titer = or < 4-Fold Maternal Titer

AND

Maternal factors:

- Treated adequately before pregnancy AND
- Low and stable nontrep titers before and during pregnancy and at delivery (VDRL < 1:2, RPR < 1:4)

Work-up/Rx:

- No evaluation needed, no Rx required (but some experts would give single dose benzathine PCN 50,000 U/KG IM, particularly if follow-up uncertain)
Congenital Syphilis
Treatment for Neonates

• Aqueous crystalline penicillin G 100,000-150,000 units/kg/d, given as 50,000 units/kg/dose IV q12 hours x 7 days, then q8 hours x 3 days (total 10 days)
  OR

• Procaine penicillin G 50,000 units/kg/dose IM qd x 10 days (only for neonates) *current drug shortage

• Single dose (ONLY for scenario 2 w/normal work-up, scenario 3 and 4): Benzathine penicillin G 50,000 units/KG/dose IM in a single dose
Evaluation and treatment of infants and children >=1 month*

- CSF analysis
- CBC, differential
- Other tests as clinically indicated

Treatment:
Aqueous crystalline penicillin G 200,000-300,000 units/kg/day IV, administered as 50,000 units/kg IV q4-6 hours x 10 days

* See CDC STD Treatment Guidelines for full details
Congenital Syphilis: Follow-up

• Serologic testing (RPR) every 2-3 months (whether treatment given or not) until test becomes nonreactive

• Nontreponemal titer should decline by 3 months and be non-reactive by 6 months if treated adequately or uninfected (may take longer if treated after neonatal period)

• Re-evaluate and treat if:
  – Nontreponemal titer persistent at 6-12 months

• If initial CSF is abnormal, repeat at 6 months. If abnormal, retreat
Patient Education Materials

Protect Yourself and Your Baby from Syphilis

What is Congenital Syphilis?
Syphilis is a sexually transmitted disease (STD). Congenital syphilis occurs when a pregnant woman with syphilis passes the infection to her unborn child. This can cause serious problems like premature birth, low birth weight, birth defects and stillbirth.

What are Symptoms of Syphilis?
Most people with syphilis have symptoms such as a sore or rash. Even if they do, they may not notice them. The only way to know for sure is to get tested! Getting tested for syphilis is part of routine prenatal care.

Who Should Get Tested?
If you are pregnant or might get pregnant, it is important to get routine prenatal care. Getting tested for syphilis and other STDs is part of routine prenatal care. Pregnant women should get syphilis testing at the first prenatal visit. Be sure to get your syphilis test results and follow any medical advice at that time.

These clinics offer FREE or LOW-COST STD testing and treatment and pregnancy planning services.

If you would like to customize and distribute within your LHJ, contact Ashley Dockter at ashley.dockter@cdph.ca.gov

Get Yourself Tested!
You can get syphilis and other STDs more than once.
If you need to get tested or would like more information on protecting yourself and your baby, talk to your health care provider, or visit a local clinic.

These clinics offer FREE or LOW-COST STD testing and treatment and pregnancy planning services.

For a complete list of free or low-cost clinics near you, visit https://gettested.cdc.gov/ or call Public Health at xxx-xxxx-xxxx.

How is Syphilis Treated?
Syphilis can be cured, even during pregnancy. Proper treatment will help prevent your baby from becoming infected.

Be sure to inform your sex partner(s) because they will need to be tested and treated too. This will help them stay healthy, avoid infecting others and avoid reinfecting you.

The clinics listed on the front of this brochure offer FREE or LOW-COST STD testing and treatment and pregnancy planning services.
Update for Health Care Providers

CONCERNING INCREASES IN SYPHILIS IN WOMEN AND CONGENITAL SYPHILIS: AN UPDATE FOR CALIFORNIA HEALTH CARE PROVIDERS

THE PROBLEM: INCREASING CONGENITAL SYPHILIS IN CALIFORNIA

California has had an increasing concern in syphilis among women over the past two years. This has been accompanied by a tripling of congenital syphilis cases from 2012 to 2014. In 2014, most female early syphilis cases and congenital syphilis cases in California were reported from the Central Valley and Los Angeles County. Most women who gave birth to babies with congenital syphilis received prenatal care late in pregnancy or not at all. This increase in numbers of congenital syphilis cases in California is an important public health problem requiring immediate attention from medical providers caring for pregnant women and women of reproductive age.

WHAT IS CONGENITAL SYPHILIS?

Congenital syphilis occurs when syphilis is transmitted from an infected mother to her fetus during pregnancy. It is a potentially devastating disease that can cause severe illness in babies including premature birth, low birth weight, birth defects, blindness and hearing loss. It can also lead to stillbirth and infant death.

CONGENITAL SYphilIS CAN BE PREVENTED

Congenital syphilis can be prevented with early detection and timely and effective treatment of syphilis in pregnant women and women who could become pregnant. Preconception and interconception care should include screening for HIV and sexually transmitted diseases (STDs), including syphilis, in women at risk, in addition to access to highly effective contraception.

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.

2. Centers for Disease Control and Prevention Syphilis Fact Sheet: http://www.cdc.gov/std/syphilis/facts.html

Version 1 (August 11, 2015)

COMMON MISTAKES

- Not reporting syphilis cases to local health departments within 24 hours.
- Not strictly adhering to treatment guidelines for pregnant women with syphilis.
- Not properly conducting routine risk assessment throughout pregnancy to determine need for additional testing.

AGNOSING SYPHILIS

Syphilis is diagnosed by reviewing patient history, taking a sexual risk assessment, physical exam, and blood tests. King the diagnosis of syphilis requires interpretation of both treponemal and non-treponemal serology tests results. Guidance on interpreting syphilis test results, refer to the CDPH screening and diagnostic guide listed in the resources for health Care Providers section.

PHILS’ TREATMENT

A treatment for a pregnant woman is based on the stage of her infection. To prevent adverse pregnancy outcomes, physicians should treat patients as soon as possible. Treating a pregnant woman infected with syphilis also treats her partner.

- Treatment for Early Syphilis (determined to be less than one year’s duration):
  - benzathine penicillin G 2.4 million units by intramuscular injection in a single dose
- Treatment for Late Latent Syphilis or Unknown Duration:
  - benzathine penicillin G 3.4 million units by intramuscular injection every 7 days for 3 weeks (7.2 million units total)

Pregnancy, penicillin is the only recommended therapy. Pregnant women with penicillin allergies should be retested and treated with penicillin. There are no alternatives.

TREATMENT AND THE ROLE OF LOCAL HEALTH DEPARTMENTS

A case with an untreated partner can cause re-infection, it is especially important to ensure that the partner(s) get treatment and to inform pregnant women about the risk to their infants if they have sex with an untreated male. Local health departments are key collaborators in the prevention of congenital syphilis, and can assist with partner treatment.

Infants born with congenital syphilis and whose mothers were not treated during pregnancy must be reported to the health department where the mother resides within 24 hours of diagnosis. Contact information for local health department staff working on syphilis treatment and reporting can be found here: http://www.cdph.ca.gov/HealthInfo/Documents/CDPH_Contact_Info.doc

SOURCES FOR HEALTH CARE PROVIDERS

Forers for Disease Control and Prevention: http://www.cdc.gov/std/syphilis


Health Advisory on Congenital Syphilis Prevention

To: San Bernardino County Providers and Hospital Maternity Personnel:

The California Department of Public Health continues to report statewide increases of syphilis among women of childbearing age (12-44 years) as well as congenital syphilis resulting from non/inadequate treatment.

San Bernardino County has been disproportionality impacted by congenital syphilis with the number of reported cases increasing by 400% from 2014 to 2016.

Prevention of Congenital Syphilis is an urgent Public Health matter.

With early diagnosis and treatment of pregnant women, congenital syphilis and its complications can be prevented.

Recommendations for all Clinicians:

1. Screen all pregnant women for syphilis at the first prenatal visit with RPR and TPPA.
2. Conduct an additional syphilis screening in the third trimester of pregnancy at 28-32 weeks.
3. Test any woman who delivers a stillborn infant for syphilis.
CDC Call to Action
Let’s Work Together to Stem the Tide of Rising Syphilis in the United States

https://www.cdc.gov/std/syphilis/resources.htm
Take-Home Points: Congenital Syphilis in California

- Female syphilis and congenital syphilis cases are increasing in California.
- Most congenital syphilis cases can and should be prevented.
- Test all pregnant women for syphilis.
- Treat syphilis as soon as possible — contact health department if challenges obtaining penicillin G and for assistance treating partners.
- Confirm syphilis testing at delivery.
- Ensure exposed infants are evaluated and treated according to guidelines.
- Follow infants until RPRs become nonreactive.
- Report syphilis to local health department within 24 hours.
- Use stdccn.org for management questions.
Hepatitis C

- Rates of hepatitis C are increasing among women of childbearing age in California
- Test pregnant women for hepatitis C if at risk
  - HIV+; ever injected drugs, even once many years ago
- Vertical transmission risk of HCV: 5% HCV+; 15-20% if HIV+/HCV+
- Currently no prophylaxis to prevent MTCT
  - Treat BEFORE pregnancy; HCV treatment not currently recommended during pregnancy
- “Perinatal hepatitis C” (hepatitis C in an infant ages 2-36 months) reportable to public health as of January 2018
- Curative HCV direct-acting antiviral treatments FDA approved for persons 12 years of age and older

Sources: Society for Maternal-Fetal Medicine Consult Series #43, Hepatitis C in pregnancy: Screening, treatment, and management.; AASLD/IDSA www.hcvguidelines.org
Follow-up and Serologic Response

- Follow-up titers should be compared to the nontreponemal titer obtained on day of treatment
  - Compare same test type, preferably same lab

- Primary and Secondary Syphilis
  - Examine at ~1 week to confirm improvement of symptoms
  - HIV-: Repeat titers at 6 and 12 months; expect fourfold decrease in serology in 6-12 months
  - HIV+: Repeat titers at 3, 6, 9, 12, 24 months

- Latent Syphilis
  - HIV-: Repeat titers at 6, 12, and 24 months; expect fourfold decrease in serology in 12-24 months (if titer initially >1:16)
  - HIV+: Repeat titers at 6, 12, 18, 24 months

CDC 2015 STD Treatment Guidelines