UC DAVIS HEALTH | CHILDREN'S HOSPITAL

Congenital Syphilis

Summary

At UC Davis Medical Center, a pediatric infectious diseases consult is required for all infants born to mothers with possible perinatal syphilis.

The following information is needed to inform appropriate evaluation and management:

- Maternal Syphilis history (i.e. dates of diagnosis, testing results (Treponemal and non-Treponemal (RPR)), and treatment(s)
    - Information from before and during the most recent pregnancy is relevant
    - Note: CDC recommends prenatal syphilis screening: during the first trimester, third trimester and at the time of delivery
    - Querying Public Health departments in counties where MOC has lived may be necessary to obtain this information -prior to contacting Public Health, collect the following maternal information:
        - Name (s)
        - DOB
        - All residing counties/cities
- Maternal risk factors for Syphilis (i.e. living in a Syphilis endemic area (this includes the UCDMC catchment area), unprotected sex, multiple partners, partner with untreated syphilis, drug use, housing insecurity, incarceration, prior STIs, limited prenatal care)
- Infant physical exam findings (i.e. small for gestational age, hepatosplenomegaly, rash, pseudoparalysis, sepsis/meningitis)
- RPR (maternal & Infant) at time of delivery
    - Note: UCD order for infants is called "RPR for congenital syphilis." Please do not order any other syphilis test for infants
- Infant follow-up
    - All infants with a positive RPR, and some with a non-reactive RPR will need outpatient Peds ID follow-up
    - Prior to discharge:
        - Please place a referral to Peds ID outpatient follow-up with Dr. Partridge
        - Please obtain the name(s) and contact information (address and phone) of guardians that baby will be discharged home with (include bio-parents if different from guardians)
        - Please discuss the need for Peds ID follow-up with guardians/bio-parents and assess for follow-up difficulties (i.e. lack of medical insurance or transportation, multiple guardians/parents etc.)

The Peds ID consulting physician will make recommendations on infant evaluation(s):

- CBC (to identify anemia, thrombocytopenia)
- LP (to identify CSF leukocytosis, elevated CSF protein, positive CSF VDRL)

- Long-bone x-rays to evaluate for osteochondritis or periostitis
- Other: CMP, eye exams

The Peds ID Consulting physician will make recommendations on infant treatment options:

- Aqueous crystalline penicillin G, IV
    - Dose:
        - 0-7 days of life: 50,000 units/kg/dose every 12 hours
        - 8 days and older: 50,000 units/kg/dose every 8 hours
    - Duration: 10 days
- Penicillin G Procaine, IM
    - Dose: 50,000 units/kg once daily
    - Duration: 10 days
- Penicillin G Benzathine, IM
    - Dose: 50,000 units/kg
    - Duration: single dose
- None

Maternal to fetal transmission of syphilis

Maternal to fetal transmission of syphilis infection can occur in utero at any trimester via transplacental transmission or during delivery via direct contact with an infected lesion.[1] The highest rates of transplacental transmission are observed in untreated mothers with primary or secondary syphilis in the third trimester of pregnancy (60-100%) compared to mothers with early latent (40%) or late latent (<8%) latent stages.[1] With the resurgence of syphilis, the use of "SCORTCH" starting with "S" for syphilis can be used as a mnemonic in the screening for intrauterine infections (SCORTCH – syphilis, cytomegalovirus, "others", rubella, toxoplasmosis, chicken pox and herpes simplex).[2] T. pallidum is not known to be secreted in breast milk.[3] There is a possibility of transmission of syphilis from direct contact with sores or skin lesions involving the nipple, areola or breast tissue during breastfeeding or breast milk expression.[4] Breastfeeding is not contraindicated and is considered safe in the absence of a lesion on the breast.[5]

Screening (testing) and management of maternal perinatal syphilis

Timely screening during pregnancy allows early diagnosis of perinatal syphilis. In areas with high prevalence of congenital syphilis or in pregnant persons with risk factors for perinatal syphilis, testing at 3 time-points during pregnancy is recommended: at the first prenatal visit, in the third trimester, and at delivery.[6] Timely testing is critical because treatment of maternal perinatal syphilis in the early stages is 98% effective in preventing congenital syphilis in the newborn.[7,8]

Syphilis screening for pregnant persons involves a combination of treponemal and non-treponemal testing. Treponemal tests such as T. pallidum particle agglutination (TP-PA), fluorescent treponemal antibody absorption test (FTA-ABS), T.pallidum enzyme immunoassay (TP-EIA) and T. pallidum chemiluminescence assay (TP-CIA) are serological tests used to detect antibodies against T. pallidum. These tests remain positive even after treatment in a majority (75-85%) of persons, and a negative test indicates the lack of infection.[9] Non-treponemal tests such as Venereal disease research laboratory (VDRL) and Rapid Plasma Reagin (RPR) detect the antibodies against biomarkers that are released from host cells following cellular damage induced by T. pallidum. Non-treponemal tests are complicated by high false positive rates especially in persons with connective tissue disorders, advanced age, lymphoma, and in infections such as Epstein-Barr virus, hepatitis, HIV, tuberculosis, malaria and measles.[1] These non-treponemal tests are used to monitor the response to treatment both in perinatal and congenital syphilis. Adequate response to treatment is indicated by a 4-fold decrease in RPR titer

within a year. In most individuals, RPR will ultimately become non-reactive several months after effective treatment, but in some individuals may remain reactive with low titers ("serofast") for years.[10] Pregnant persons who are seropositive are infected unless they have documentation of adequate treatment with appropriate serologic response to treatment and RPR titers are low (RPR <1:4) and stable.[1] Persons with up-trending or persistent high antibody titers may indicate reinfection.[1]

Comprehensive, non-judgmental care is encouraged for perinatal syphilis. Maternal treatment involves either single dose of intramuscular (IM) penicillin (2.4 million units benzathine penicillin G) in the early stages of infection (primary, secondary, or early latent) or three weekly doses of penicillin for late latent or tertiary syphilis. Neurosyphilis warrants 10-14 days of intravenous (IV) aqueous penicillin. Pregnant persons who are allergic to penicillin should undergo desensitization and subsequent treatment with penicillin due to lack of alternate therapy.[11] Contact tracing and treatment of partners is crucial in preventing reinfection in the pregnant person. Per the WHO, untreated syphilis during pregnancy can result in adverse birth outcomes in 50-80% of cases [12].

Symptoms and signs of congenital syphilis

Congenital syphilis infection is classified as early or late based on the onset of clinical symptoms. Large, thick and pale placenta and abscess-like foci of necrosis in Wharton's jelly centered around the umbilical vessels (necrotizing funisitis with "barber-pole appearance") can be observed in congenital syphilis. Early congenital syphilis presents within the first 2 years of life, but most commonly within 3 months after delivery. The symptoms of early congenital syphilis range from asymptomatic (~70% of cases) to stillbirth (up to 40% in untreated pregnancies) and include hydrops fetalis and preterm delivery (figure 1).[1] Other symptoms of congenital syphilis are pneumonia, "snuffles" or nasal congestion and excessive nasal discharge, hepatosplenomegaly, lymphadenopathy, hyperbilirubinemia, cholestasis, or maculopapular, desquamating rash that can involve the palms and soles. Central nervous system involvement can present with meningitis, seizures, hearing loss and rarely uveitis and optic atrophy.[9] Infants with congenital syphilis can have skeletal system involvement in the form of osteochondritis or periostitis, with or without pseudoparalysis of parrot (decreased range of movement due to painful periostitis).[10] Hypoxic ischemic encephalopathy, persistent pulmonary hypertension of the newborn and disseminated intravascular coagulation have also been reported.[13]

Untreated asymptomatic infants with congenital syphilis infection may present with clinical features after 2 years of age resulting in late congenital syphilis.[1] The clinical presentation at this stage includes the triad of congenital syphilis: interstitial keratitis, sensorineural hearing loss, and notched central incisors or Hutchison teeth. Furthermore, they may develop anterior bowing of shin (saber shin), painless swelling of the knee (Clutton joints), mulberry molars (rudimentary cusps in first molars), saddle nose, and developmental delays.[9] Renal disease in the form of glomerulonephritis and nephrotic syndrome have been reported as well.[14]

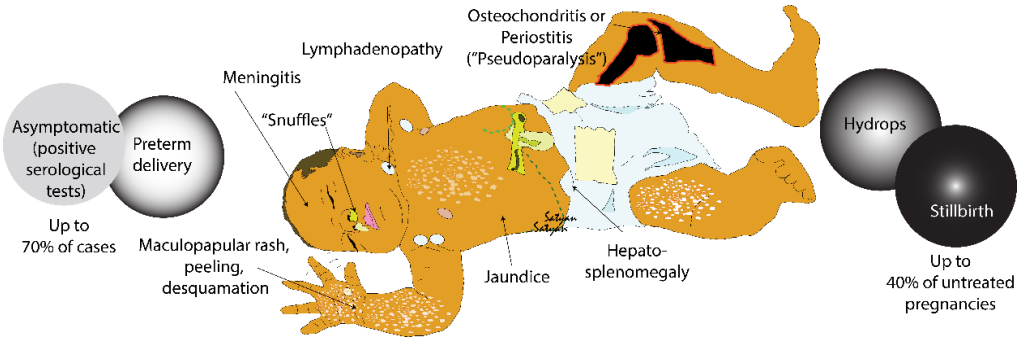

Figure 1: Clinical features of congenital syphilis.

Diagnosis and management of congenital syphilis

The Centers for Disease Control and Prevention (CDC) and American Academy of Pediatrics (AAP) have published guidelines to assist providers with the diagnosis and management of congenital syphilis. Key points from these guidelines are as follows (see Table 1 and Figure 2):

1. All infants born to mothers with a known perinatal syphilis infection or positive syphilis screening (combination treponemal and nontreponemal) during pregnancy or at delivery should undergo screening for congenital syphilis prior to discharge from the birth hospital.
2. The screening test for congenital syphilis is a nontreponemal (RPR) test.
3. Infants with physical exam findings concerning for congenital syphilis or RPR titer ≥4-fold maternal titer should have a workup (inclusive of cerebrospinal fluid/CSF analysis for cell count, protein, and CSF-VDRL; complete blood counts (CBC) and long-bone radiographs). These infants should receive 10 days of IV aqueous penicillin regardless of the workup results.
4. Infants with a normal physical exam, RPR titer <4-fold maternal titer, and mother with no treatment or treatment unknown, inadequate or initiated <30 days prior to delivery, should undergo a workup (inclusive of CSF analysis for cell count, protein, and CSF-VDRL; complete blood counts (CBC) and long-bone radiographs). If any part of the work-up is abnormal, uninterpretable, or incomplete, the infant should receive 10 days of IV aqueous penicillin. If the workup is normal, interpretable, complete, and follow-up for repeat RPR at 2 to 3 months is certain, the infant should receive a single dose of IM Benzathine penicillin.
5. Infants with a normal physical exam, RPR titer <4-fold maternal titer, and a mother who received treatment for perinatal syphilis infection that was adequate for maternal stage of infection, initiated >30 days before delivery with no concern for reinfection, no further workup is recommended. If follow-up for repeat RPR at 2 to 3 months after birth is uncertain, the baby can receive a single dose of IM Benzathine penicillin. No treatment is recommended if outpatient follow-up for repeat RPR in 2- 3 months is assured.
6. Infants with a normal physical exam, RPR titer <4-fold maternal titer and a mother who received adequate treatment for the maternal stage of infection prior to pregnancy with no concern for reinfection, no further workup or treatment is recommended for the infant. For babies with reactive RPR and for whom follow-up for repeat RPR at 2 to 3 months after birth is not certain, a single dose of IM Benzathine penicillin could be administered.
7. All infants with positive RPRs at birth or with a negative RPR but concern for possible incubating congenital syphilis should have follow-up RPR testing at 2 to 3 months after birth.

Table 1. Adapted evaluation and management guidelines based on CDC and AAP risk-stratification algorithms.

Table adapted from Fang et al. (https://creativecommons.org/licenses/by/4.0/). CSF, cerebral spinal fluid; CBC, complete blood count; RPR = rapid plasma reagin; VDRL, Venereal Disease Research Laboratory Test. * Other tests as clinically indicated (e.g., liver function tests, neuroimaging, ophthalmologic exam, and auditory brain stem response).

Scenario (CDC) Risk Category (AAP)	Clinical History and Examination	Evaluation	Treatment
Scenario 1, Category: Confirmed proven or highly probable congenital syphilis	Abnormal physical exam OR RPR titer ≥4-fold maternal titer	CSF analysis (cell count, protein, VDRL), CBC, long bone radiographs, Other *	Intravenous Penicillin G × 10 days (regardless of evaluation results)
Scenario 2, Category: Possible congenital syphilis	Normal physical exam AND RPR titer <4-fold maternal titer AND Maternal treatment none/unknown/inadequate or initiated <30 days before delivery	CSF analysis (cell count, protein, VDRL), CBC, long-bone radiographs	Penicillin G x 10 days (if evaluation is abnormal, uninterpretable, incomplete, or follow-up uncertain) OR Intramuscular Benzathine Penicillin × 1 (if evaluation and follow-up certain)
Scenario 3, Category: Less likely congenital syphilis	Normal physical exam AND RPR titer <4-fold maternal titer AND Maternal treatment: adequate and initiated ≥ 30 days before delivery and no concern for reinfection	None	Intramuscular Benzathine Penicillin × 1 (if follow-up uncertain) OR No treatment with follow-up titers (if follow-up certain)
Scenario 4, Category: Unlikely congenital syphilis	Normal physical exam AND RPR titer <4-fold maternal titer AND Maternal treatment adequate before pregnancy	None	No treatment with follow-up RPR titers (if infant RPR positive) OR Intramuscular Benzathine Penicillin × 1 (if follow-up uncertain)

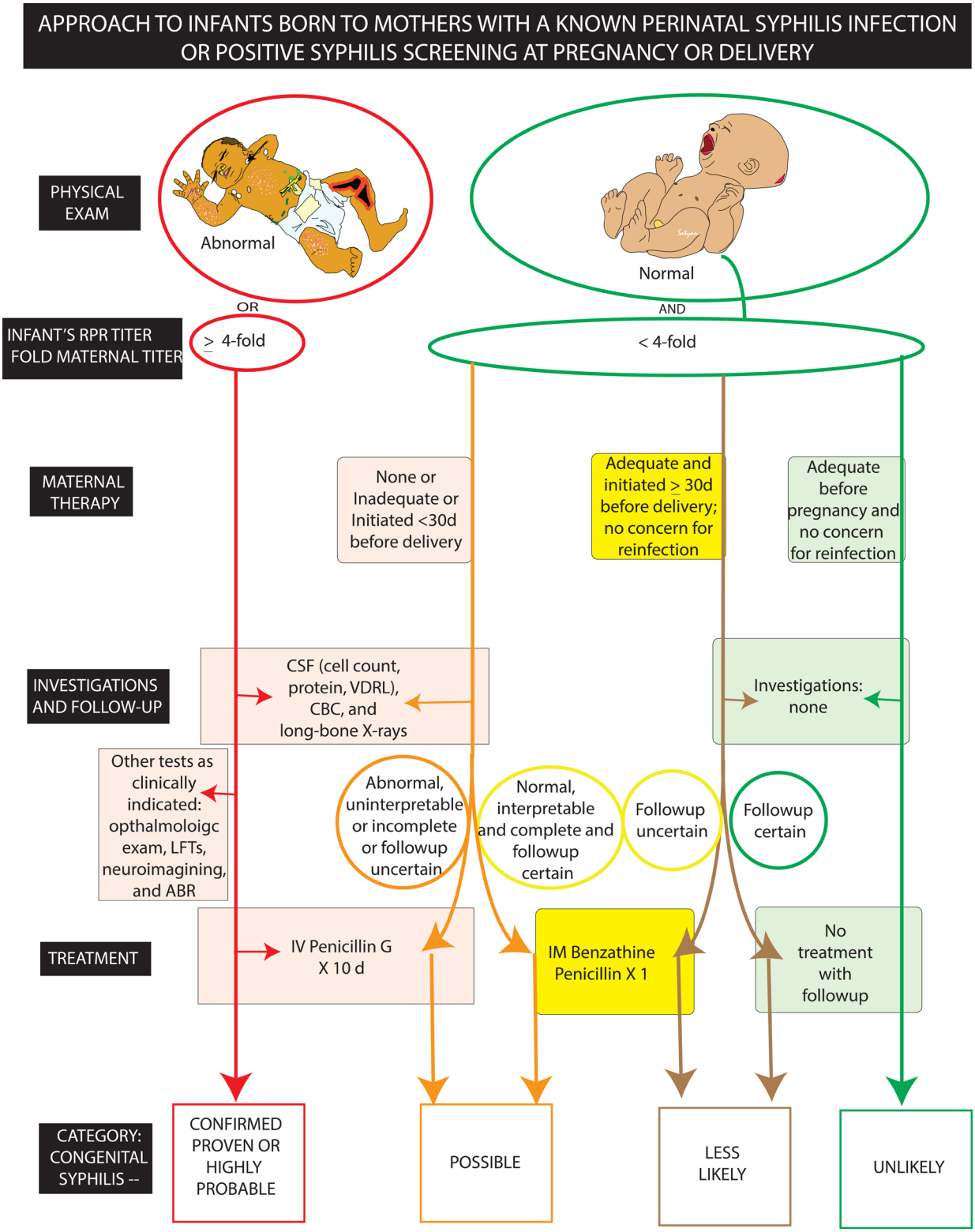

Figure 2: Screening and management algorithm for congenital syphilis. CSF, cerebrospinal fluid. RPR, rapid plasma reagin. CBC, complete blood counts. LFT, liver function tests. ABR, auditory brainstem response for hearing test.

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