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Clinical Guidance:
Infant and Child Follow-up After Exposure to Syphilis in Utero

CAPTC

Who needs follow-up:

- **Panel A**: Neonates (aged < 30 days) including:
  - Neonates with reactive RPR/VDRL at delivery
  - Neonates with non-reactive RPR/VDRL at delivery but the mother continues to have reactive RPR/VDRL despite adequate prior treatment
- **Panel B**: Infants and children (aged ≥ 30 days) who were treated for congenital syphilis at or after 30 days of age

Panel A: Follow up for neonates (aged < 30 days) when the neonate and/or mother has a reactive RPR/VDRL at delivery

Neonatal RPR/VDRL reactive

Neonate required treatment for congenital syphilis
- See CDC guidelines for treatment decision-making
- Treatment may include IV PCN for 10 days or IM PCN once

RPR/VDRL every 2 - 3 months

- Reactive at 12 months of age (1)
  - **Possible treatment failure:**
    - CSF examination
    - Expert consultation
    - Consider retreatment with IV PCN for 10 days
- Non-reactive before or at 12 months of age
  - **Stop checking RPR/VDRL**; no additional testing or treatment needed

Neonate did not require treatment for congenital syphilis
- See CDC guidelines for treatment decision-making

RPR/VDRL every 2 - 3 months

RPR/VDRL should decrease by 3 months of age (2)

- Reactive at 6 months of age
  - **Likely congenital syphilis:**
    - CSF examination
    - Expert consultation
    - Consider treatment with IV PCN for 10 days
- Non-reactive at or before 6 months of age
  - **Stop checking RPR/VDRL**; no additional testing or treatment needed

Neonatal RPR/VDRL non-reactive but maternal RPR/VDRL reactive despite adequate treatment prior to delivery

Neonate not treated for congenital syphilis (3)

RPR/VDRL at 3 months of age

- RPR/VDRL reactive
  - **Likely incubating congenital syphilis:**
    - CSF examination
    - CBC with differential & platelets
    - Long-bone radiographs
    - Other tests as indicated
    - Expert consultation
    - Consider treatment with IV PCN for 10 days
    - If exam and all workup is normal, consider IM PCN once weekly for 3 weeks
- RPR/VDRL non-reactive
  - **Stop checking RPR/VDRL**; no additional testing or treatment needed

Panel B: Follow up for infants and children (aged ≥ 30 days) who are treated for congenital syphilis at or after 30 days of age

Note: Follow-up recommendations here are for infants and children who were evaluated and treated for congenital syphilis after the neonatal period (aged ≥ 30 days). For those infants and children newly identified as having a reactive RPR/VDRL, there should be a thorough exam and review of maternal serology and records to assess if they have congenital or acquired syphilis. Any infant or child at risk for congenital syphilis should receive a full evaluation as well as testing for HIV infection. Please refer to CDC guidelines for evaluation and management of non-perinatally acquired syphilis.

RPR/VDRL every 3 months following treatment with either IV PCN for 10 days or IM PCN once weekly for 3 weeks

- Increase in titers (≥ fourfold) at any point for > 2 weeks (4)
- RPR/VDRL not decreased by ≥ fourfold after 18 months (1)

  Possible treatment failure:
  - Re-evaluate with CSF examination
  - Expert consultation
  - Consider retreatment with IV PCN for 10 days
- Non-reactive RPR/VDRL or ≥ fourfold decrease at or before 18 months
  - **Stop checking RPR/VDRL**; no additional testing or treatment needed

1. CDC recommends re-evaluation with CSF examination and management in consultation with an expert for treated neonates (Panel A) who exhibit persistent RPR/VDRL titers by 6-12 months and treated infants or children (Panel B) whose RPR/VDRL titers do not decrease ≥ fourfold by 12-18 months. By expert opinion, it is reasonable to wait the full 12 months (for neonates) or 18 months (for infants) before repeating a lumbar puncture if RPR/VDRL titers are down-trending appropriately after treatment.
2. CDC does not provide guidance for what actions to take if RPR/VDRL does not decrease by 3 months of age. Based on expert opinion, if RPR/VDLR is unchanged (within 2-fold above or below the birth titer) by 3 months of age, consider providing benzathine penicillin G 50,000 units/kg body weight/dose IM once.
3. CDC recommends all neonates with a negative RPR/VDRL at delivery whose mothers are seroreactive be retested at age 3 months to rule out serologically negative incubating congenital syphilis. Based on expert opinion, any neonate with a normal physical exam, non-reactive RPR/VDRL at delivery, whose mother was treated adequately before delivery, and who received treatment (e.g., IM PCN once) does not need follow-up RPR/VDRL at 3 months of age.
4. CDC does not quantify significant titer increase for infants and children. It is expert opinion that significant increases are ≥ fourfold, the same as adults/adolescents.

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Narrative

Neonates, infants, and children exposed to syphilis during pregnancy require close follow-up, which should continue until there is no longer concern for ongoing infection (see page 1 for details). Follow-up can be complicated as maternal treponemal and non-treponemal antibodies are transferred vertically and may persist for more than a year after delivery.

This tool provides algorithms and guidance on recommended titer frequency, titer interpretation, additional evaluation, and treatment in infants and children in concordance with the CDC STI Treatment Guidelines. Expert opinion is added to provide clarity when appropriate (see footnotes). For guidance on the initial diagnosis or treatment of congenital syphilis, please see the CDC STI Treatment Guidelines and the California Prevention Training Center Congenital Syphilis Algorithm.

The details of infant and child follow-up after exposure to syphilis in utero are determined by several factors, including: (1) age at which syphilis exposure is identified, (2) newborn syphilis titers at time of delivery, (3) whether the baby was treated for syphilis exposure, and (4) titer response in the months following treatment. In addition to the follow-up recommendations presented in this document, there are several general principles to which clinicians should adhere when caring for such patients:

- The same type of non-treponemal test (RPR or VDRL) should be used each time for follow-up testing. RPR titers tend to be slightly higher than VDRL titers and results from different tests cannot be directly compared.
- Treponemal tests (e.g., EIA, CIA, TP-PA, etc.) should not be used to evaluate treatment response because results are qualitative and persist after treatment. Passive transfer of maternal IgG antibodies might persist for more than 15 months after delivery.
- Neonates (< 30 days old) and infants (≥ 30 days old) with abnormal CSF at initial evaluation and treatment do not need repeat lumbar punctures unless serum RPR/VDRL titers are reactive at 6-12 months for neonates or RPR/VDRL titers do not decline ≥ fourfold by 12-18 months for infants. Based on expert opinion, it is reasonable to wait the entire 12 months (for neonates) or 18 months (for infants) before repeating a lumbar puncture if RPR/VDRL titers are down-trending appropriately after treatment.
- The work-up for congenital syphilis always includes CSF analysis, complete blood count with differential and platelets, and long-bone radiographs. Other tests as clinically indicated may include chest radiographs, liver function tests, abdominal ultrasound, ophthalmologic examination, neuroimaging, and auditory brainstem response.
- For neonates with non-reactive RPR/VDRL born to mothers with newly reactive treponemal and reactive RPR/VDRL serology who never received treatment or had inadequate treatment prior to delivery – evaluation, treatment, and follow-up for congenital syphilis should proceed as if the neonate's RPR/VDRL was reactive at birth.
- For neonates with non-reactive RPR/VDRL born to mothers with reactive treponemal tests but non-reactive RPR/VDRL (e.g., maternal EIA reactive, RPR non-reactive, and TP-PA reactive) due to syphilis treatment before pregnancy – congenital syphilis is unlikely. See CDC guidelines, Scenario 4, for treatment recommendations. Follow-up RPR/VDRL for the infant should be considered at 3 months of age if syphilis exposure prior to delivery could not be ruled out.
- Syphilis is unlikely for neonates delivered by mothers screened with the reverse sequence algorithm when maternal results show isolated reactive treponemal serology (e.g., EIA reactive, RPR non-reactive, and TP-PA non-reactive). Among low-prevalence populations, these are likely false-positive results and might become non-reactive with repeat testing. If these neonates have a normal physical exam and the risk for syphilis is low in the mother, no follow-up is needed for the neonate.

Congenital syphilis recognition, treatment, and follow-up is complicated and there may be unique scenarios that are not well described by this clinical tool. Consider contacting your institutional pediatric infectious disease provider if questions arise. If no such expert is available or additional guidance is needed, questions can be directed to your local/state health department or the Sexually Transmitted Diseases Clinical Consultation Network.