

CONTAGIOUS COMMENTS

Department of Epidemiology

Congenital Syphilis Rates on the Rise: What Do We Do?

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What is Syphilis and Why Does It Matter?

Syphilis, or versions of it, have been described for centuries. Why are we bringing it up now? Rates of infection with this spirochetal organism, *Treponema pallidum*, have been rising significantly over the past 10 years without slowing. We typically think of syphilis as a sexually transmitted infection (STI), with the highest rate of disease in adults occurring in men who have sex with men (MSM).² However, the rate of primary and secondary syphilis in women of childbearing age (15-45 years) is rising at an incredible slope, particularly in Colorado. From 2018-2022 in Colorado, rates of diagnosed cases of syphilis in women in this group increased by 523% from 11.2 to 69.9 diagnoses per 100,000 people, respectively.³⁻⁶ In 2023, 28% of the cases of syphilis in Colorado that were reported in women of childbearing age were acquired during pregnancy, an increase from 23% the year prior. Importantly to providers caring for infants and children, vertical transmission of the spirochete can occur from mother to infant if the mother has not been treated or has been inadequately treated. As would follow, congenital syphilis increased seven-fold in Colorado from 2018-2023. Most alarmingly, CDPHE reported in a Health Alert Network Message on April 1, 2024 that in the first three months of 2024 (January through March), there were 22 reported congenital syphilis cases. In the same timeframe in 2023, there were only 6 cases reported.⁶

Manifestations of congenital syphilis range from stillbirth to preterm delivery to live birth with morbidity; however, just as concerning is that about half of the infants born with congenital syphilis are born without signs or symptoms of infection. Availability and evaluation of the mother's records is therefore imperative since infants with untreated congenital syphilis may develop sequelae of disease later in childhood.

Testing Recommendations for Women of Childbearing Age in Colorado

The 2021 CDC STI guidelines recommend testing of all pregnant women for syphilis at least at the first prenatal visit. They also add that if the pregnant woman lives in an area where there is a high syphilis rate or if she has risk factors for acquiring the infection (e.g., STI during pregnancy, multiple sex partners, misuse of drugs) that she should be retested at 28 weeks gestation and again at delivery. Each year, CDC evaluates missed opportunities in maternal care that may have led to infants born with congenital syphilis. The 2022 report concluded that of the 3,755 cases of congenital syphilis for which data were available, 37% of the cases were due to no timely syphilis testing, with another 50% of women that did not receive treatment (11% of all cases) or received inadequate treatment (39% of all cases) even if a test was done in a timely manner.^{2,9} Of the infants with congenital syphilis born in 2022, about 1/3 of mothers had no documented prenatal care.⁹ Multiple reasons may explain these trends, which include difficulties accessing prenatal care due to social, economic, and cultural barriers such as experiencing homelessness and/or substance abuse.^{12,13} However, another important finding from a CDPHE analysis of the Colorado cases of primary or secondary syphilis in women of reproductive age during 2017-2022 is that 52% of the cases in this group had no known social factors typically associated with increased risk of syphilis infection, emphasizing the need to test more than those with "high risk" behavior.^{5,6}

The newest recommendation for Coloradans released in an April 1, 2024 CDPHE HAN⁶ (now as a Public Health Order effective April 25, 2024⁷) is for **all** pregnant people to have testing *three times* during pregnancy – at the first prenatal visit, early in the third trimester, and again at delivery, regardless of risk factors.⁶ To address the issue of individuals who may not have sought prenatal care, CDPHE provided additional guidance for emergency departments and urgent cares to ensure that providers review the syphilis testing status of any pregnant woman if she presents to care.^{5,6} If no testing during pregnancy has been done or documentation is not available, providers should test for syphilis while in their care. In some cases, a stat RPR card test may be available for rapid diagnosis providing an opportunity for identification and treatment of a pregnant woman during the same encounter, thus potentially preventing congenital syphilis.¹⁷

So, what is our role as providers caring for infants and children?

- **Acknowledge** the epidemiology of primary and secondary syphilis in Colorado to identify symptomatic adolescents and those who should be routinely screened for syphilis
- **Understand** how to review mother's test results and treatment history

- **Identify** the signs or symptoms of missed congenital syphilis in older infants and children
- **Use and follow** the AAP recommendations for evaluation and diagnosis of congenital syphilis

When to Consider Congenital Syphilis

Newborn Nursery/NICU

The ideal time for diagnosis and treatment of syphilis or congenital syphilis is *before* a woman becomes pregnant, but identification during pregnancy is just as important. For providers, that means the first time we can evaluate for exposure to syphilis is while the infant is still in the newborn nursery or NICU. This is also the time at which we have the most access to the mother's medical record.

Outpatient/ED

With half of patients with congenital syphilis born without symptoms, diagnosis can be missed if maternal testing is not evaluated before or at delivery. Case reports have described children presenting with unusual fractures who undergo workup for non-accidental trauma (NAT) but are ultimately found to have untreated congenital syphilis. In patients presenting with unusual fractures, missed congenital syphilis could be considered in the differential for NAT. Otherwise, the presentation of infants and children with untreated congenital syphilis may vary, but can include fever, hepatomegaly, rash involving the palms and soles or ulcerative skin lesions, or rhinitis (snuffles) in addition to the aforementioned pathologic fractures.

Making the Diagnosis

The most important pieces of information for evaluation of congenital syphilis are maternal screening test results with dates, maternal treatment documentation, and our exams. The first two items are contingent on this work being done and documented in the mother's chart, but also upon ability to gain access to these records, which is why it is helpful to do this evaluation while the infant is still in the nursery when we have the best access to maternal records. Even so, obtaining this information can be time-consuming, particularly when testing or treatment is done outside of the same healthcare system.

Evaluation of Maternal Testing and Treatment

The current Public Health Order for Colorado requires that healthcare facilities "take all necessary steps to offer and provide" syphilis screening for pregnant women in the 1st and 3rd trimesters, as well as at delivery without consideration for risk factors.^{6,7} The type of test done and the testing dates are critical to know, particularly given the complexity of the tiered testing system for syphilis. With no new testing modalities available for syphilis in decades, a multi-tiered system for evaluation remains the mainstay of diagnosis. Both types of test, treponemal and non-treponemal Ab tests, have pros and cons (see Table 1), but together provide a reliable testing mechanism for diagnosis, with some caveats, and remain the recommended way to evaluate for syphilis.^{8,10,11,16}

Conventional algorithm: Some healthcare systems still use the conventional testing algorithm that begins with a non-treponemal test such as RPR or VDRL (see Table 1), followed by confirmatory testing with a treponemal test (e.g., FTA-ABS; Table 1) if the first test is positive. If the follow-up test is negative, in most cases the positive RPR would be considered a false positive.^{1,8,10,11,16}

Reverse-sequence algorithm: Many larger healthcare systems have moved to the reverse sequence testing algorithm. In this case, the first line test is treponemal Ab testing, which allows for faster throughput of tests in larger numbers. A positive treponemal Ab test, however, may represent current or past/treated infection – in most cases, it may remain positive for life. Reflex testing to a non-treponemal test is therefore required. If this is negative, a third evaluation is recommended with a *different* Treponemal Ab test than was initially done (e.g., if EIA was done initially, TP-PA could be done). With this more complex algorithm, it is imperative to understand what these results mean and ensure that the appropriate test types were done before evaluating an infant for congenital syphilis.^{1,8,10,11,16}

With respect to maternal treatment, we must confirm when a woman was treated for known syphilis with documentation review; verbal report is not acceptable. Again, this can be quite a challenge, particularly if this occurred out of state. Typically, though, cases of syphilis are reported to the department of public health where a person is living, so documentation may be

Table 1. Treponemal vs Non-treponemal tests^{8,10,11,16}

Treponemal Ab test	Non-treponemal (lipoidal) Ab test
<ul style="list-style-type: none"> • EIA • CIA • FTA-ABS • TP-PA 	<ul style="list-style-type: none"> • RPR • VDRL
Pros: <ul style="list-style-type: none"> • Faster throughput • Tests can be batched; more tests run at once • May be more sensitive in early primary syphilis 	Pros: <ul style="list-style-type: none"> • Can monitor for response to treatment • Becoming more automated
Cons: <ul style="list-style-type: none"> • Positive typically for life (cannot use for response to treatment) • False positives in other spirochete infections 	Cons: <ul style="list-style-type: none"> • Considered more manual • False positives in autoimmune disease, EBV, measles, endocarditis, malignancy (non-exhaustive list)

able to be obtained from these organizations. The CDPHE Syphilis Case Ascertainment Unit may also be able to assist with obtaining this information⁷. Evaluation of this documentation is helpful in understanding whether the mother has had evidence of response to the prescribed therapy, which can be noted by evaluation of decrease in the non-treponemal Ab titer (e.g., RPR).

Physical Exam

Infants with congenital syphilis can have a broad range of physical exam findings at birth, from no abnormalities on examination to respiratory failure, hydrops, or stillbirth. Within that range can be specific findings of rash, hepatomegaly, splenomegaly, broadened nasal bridge, or pseudoparalysis due to periostitis or osteochondritis (specifically in long bones). Ophthalmologic exam can reveal chorioretinitis and long bone x-rays can show radiographic evidence of periosteal reaction, diffuse or localized osteitis, and metaphysitis, which can be clues for congenital syphilis.^{1,15}

If patients with untreated congenital syphilis present later in life, physical exam findings can include bone pain (from pathologic fracture) or bowing of the shin (saber shin), snuffles (rhinitis with mucus), rash (many presentations, but can be maculopapular and present on palms and/or soles), interstitial keratitis or uveitis, or sensorineural hearing loss.^{1,14,15}

Regardless of treatment for congenital syphilis, patients born with this infection may see Hutchinson teeth when secondary teeth come in. This manifests as notched or peg-shaped central incisors.

Laboratory Evaluation¹

As discussed above, assays to evaluate for syphilis (and congenital syphilis) have not changed in decades. Diagnosis of congenital syphilis is therefore made by likelihood of an infant having the infection after review of maternal testing and treatment information, and decisions on whether that information warrants testing of the infant. If there is evidence that maternal infection has not been treated, has been treated but treatment was given too close to delivery, has been inappropriately treated, has been treated without effective response or if there is concern for reinfection during pregnancy, or treatment documentation cannot be evaluated, recommendations are to evaluate the infant. This evaluation takes into consideration the multiple organ systems that can be affected by infection with *T. pallidum*, as well as the infant's response to maternal infection. Of note, if the mother declines testing for herself, non-treponemal Ab test should be sent from the infant.

Laboratory evaluation of an infant for which there is concern for congenital syphilis includes a complete blood count (CBC) with differential; complete metabolic panel (CMP); lumbar puncture with cerebrospinal fluid (CSF) analysis of red and white blood cell counts, protein, and glucose; and non-treponemal blood and CSF Ab testing with titer. CBC may reveal leukocytosis or thrombocytopenia while the CMP may demonstrate elevated AST, ALT, or bilirubin. Evidence of CSF pleocytosis, particularly with elevated protein, may be an indicator of neurosyphilis.

The infant's non-treponemal antibody titer should be compared to the mother's. It is therefore important that the same non-treponemal test is done on the infant that was done for the mother, so they can be compared. On the other hand, CSF VDRL is the antibody test of choice for evaluation for neurosyphilis, acknowledging the potential for false-negatives and false-positives (particularly in the case of a bloody lumbar puncture).

Treatment

Treatment of congenital syphilis¹

Congenital syphilis treatment protocols are stratified based on the likelihood that the infant has congenital syphilis. In proven or highly probable congenital syphilis, a 10 day course of penicillin G is recommended without exception. A course of IV or IM penicillin G should be administered, ensuring that the appropriate formulation is used for the appropriate administration modality (e.g., aqueous crystalline penicillin G should be administered IV intermittently through the day and procaine penicillin G can be administered IM once daily for the duration). However, if the infant is diagnosed with *possible* congenital syphilis based on the AAP Red Book algorithm, if congenital syphilis is less likely, and in some cases if congenital syphilis is deemed unlikely, there is some flexibility for administration of a single dose of IM benzathine penicillin G depending on the clinical scenario, likelihood of follow up, and other social determinants.

In the case of an infant with a positive CSF VDRL and/or cell counts concerning for neurosyphilis, the treatment duration remains the same. Diagnosis of neurosyphilis should prompt additional imaging and neurodevelopmental follow up.

Treatment of syphilis in pregnant women

Penicillin G is the only form of syphilis treatment that has been studied well enough to demonstrate effective treatment of infants *in utero* for syphilis. It is therefore the only treatment of choice for prevention of congenital syphilis. Pregnant women must be treated at least 30 days prior to delivery of the infant to decrease the chance that the infant will have active infection at birth; however, even if the mother was treated, evaluation of the infant's RPR and a careful physical examination of the infant must be done to stratify the likelihood of the infant having congenital syphilis.^{1,17}

Notably, there are sporadically periods of penicillin G shortages (most recently, an IM benzathine penicillin G shortage), in which case many healthcare settings experiencing this shortage have prioritized use of existing stocks for pregnant women only (IM formulations) or infants born with congenital syphilis (IV formulations). Alternative agents to treat other diagnoses (e.g., Group A Strep infection) or for treatment of syphilis in non-pregnant individuals is emphasized for preservation of the supply for pregnant women.

In situations where an antimicrobial other than penicillin G has been used in a pregnant woman, for purposes of diagnosing congenital syphilis, the mother is considered inappropriately treated.

Outpatient Management Following Treatment

AAP Red Book recommendations for outpatient management of patients who have been treated with congenital syphilis have been revised as of the 32nd edition and remain the same for the 33rd edition coming out in 2024.¹ Infants should already have had hearing screen. After discharge, infants should be evaluated with a thorough physical exam at each of the scheduled well child checks. New signs of infection are unexpected in an appropriately treated child. However, the infant's response to therapy should be documented by performing RPR or VDRL (whichever was done for diagnosis) every 2-3 months until negative. If this test is not decreasing by 6 months or not negative by 6-12 months, re-evaluation and re-treatment for syphilis should be considered.

It is also helpful to provide anticipatory guidance to parents of patients who are diagnosed with and treated for congenital syphilis. This can be guided in part by the findings of the patient's evaluation at diagnosis. Sensorineural hearing loss should have already been screened for by discharge. Provide guidance about the possibility of Hutchinson teeth with emergence of secondary teeth. Watch for long bone length discrepancies given involvement of metaphyses in periostitis. Patients with neurosyphilis should also be followed closely for developmental delays.

Syphilis Screening and Treatment in Adolescents

Finally, while the 2021 STI Guidelines do not recommend compulsory testing for syphilis in sexually active adolescents, given the significant rate of rise of primary and secondary syphilis in women of childbearing age in Colorado, the April 2024 CDPHE HAN recommends syphilis screening for any person being evaluated for a sexually transmitted infection. This testing includes syphilis, HIV, gonorrhea, and chlamydia.^{6,17} This includes testing of all sexually active people 15-44 years of age. Treatment of the patient should be promptly pursued, as well as of any sexual partners.

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