



INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: Congenital Syphilis
-November 2024-



Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) conducted an overview of Congenital Syphilis. Medication listed on the National Core Formulary (NCF) relevant to this condition includes [Benzathine Penicillin G](#). Following this clinical review, the NPTC made **no modifications** to the NCF.

Discussion:

Congenital Syphilis (CS) is the disease that occurs when a pregnant person with syphilis passes the infection on to the fetus during pregnancy. *Treponema pallidum* is transmitted in-utero directly to the fetus' bloodstream and causes widespread infection and inflammation to organ systems. CS can result in miscarriage, neonatal death, preterm delivery and long-term health problems in the affected child.¹ CS is preventable, treatable, and curable.

Epidemiology: Syphilis, including CS, is a national public health crisis. Significant disparities by race and ethnicity persist with AI/AN having the highest rates of syphilis, maternal syphilis (MS) and CS.² 2023 CDC data: 10,121 maternal syphilis cases with a rate of 280.0 cases /100,000²; AI/AN rate is 1,410 cases /100,000.² 2023 CDC data: 3,882 CS cases² with a rate of 102.5 cases /100,000;² AI/AN rate is 644.7 cases /100,000.²

Maternal Syphilis: Diagnosis and treatment of syphilis before pregnancy prevents CS.³ Early identification of syphilis during pregnancy and timely treatment with the appropriate benzathine penicillin G regimen can prevent 98% of CS cases.³ CS may be contracted at any stage of MS and in any trimester of pregnancy.^{4,5} 40% of untreated first trimester syphilis results in spontaneous abortion, stillbirth, or perinatal death.^{4,5} Untreated pregnant persons have an 80% chance of passing syphilis to their infants.^{3,4} Transmission rates: 60-100% for 1^o and 2^o; ~40% early latent; 8% for late latent.⁵ Lack of timely testing and adequate treatment during pregnancy contributes to 88% of CS cases across the USA.⁷

Maternal Testing and Treatment: April 2024 updated guidelines from The American College of Obstetricians and Gynecologists (ACOG): **all** pregnant individuals should be tested serologically for syphilis **three times**; at the first prenatal care visit, during the third trimester, and at birth.⁸ Per 2024 CDC guidelines, either diagnostic pathway is acceptable.⁹ Pregnancy does not change the diagnosis, course, or treatment of syphilis.⁶ Penicillin (PCN) is the only known effective antimicrobial for treating MS and preventing CS.¹⁰ Those allergic to PCN should be desensitized and then treated.¹⁰

Congenital Syphilis: The American Academy of Pediatrics (AAP) has stated that “No mother or newborn infant should leave the hospital without maternal serologic status having been documented.”¹¹ Infants whose mothers had known perinatal syphilis or a positive syphilis screen require evaluation. Initial assessment includes physical exam, the infant's non-treponemal ratio and adequacy of the mother's treatment. Neonatal algorithms guide additional testing, risk category and treatment regimen.^{4,5,11,12} Treatment of the infant is with PCN; the regimen is based on the risk category of CS.^{4, 12}

Evaluation Information: (1) Infants require a non-treponemal test performed on the infant's serum. Maternal treponemal antibodies can cross to the baby; hence neither treponemal testing nor cord blood is used for infant testing.^{4,5,11} (2) Any infant for whom there is a CS concern requires a lumbar puncture. Abnormal cerebrospinal fluid tests require the 10-day IV penicillin G treatment course as benzathine PCN does not penetrate the blood-brain barrier adequately.^{4, 5, 11} (3) Antibiotics given in-hospital for sepsis concern (such as ampicillin) do not count toward the 10-day treatment course for CS.⁴

Pediatric Follow-Up: includes serology, careful well child exams, yearly hearing and vision screenings, serial developmental testing and follow up of known complications of CS.^{12,13} Serology is completed every 2-3 months until non-reactive;¹¹ this should occur by 6 months of age. If not declining, re-evaluation and possible re-treatment are indicated¹¹.

Congenital Syphilis Continues to be Undiagnosed at Birth. It is important for pediatric providers to review birth records, maternal syphilis status and adequacy of maternal treatment at the first visit for every infant. Clinical presentation in early CS (\geq 1 month–2 years) ranges from asymptomatic (70%) to nonspecific concerns (small for gestational age, fever, poor feeding, low weight gain, jaundice, anemia, rash, meningitis) to overt manifestations (snuffles-syphilitic rhinitis, syphilitic bony lesions).^{4,5,13} Clinical presentations in late CS (>2 years) may include the central nervous system (intellectual difficulties, deafness), orthopedics (Saber shins, Clutton joints), facial (frontal bossing, saddle nose, rhagades), teeth (Hutchinson teeth, Mulberry molars), eye (interstitial keratitis, optic nerve atrophy, healed chorioretinitis) and others.^{4, 5, 13} Evaluation of the older infant/child is similar to the neonate.^{4,12} Treatment is intravenous PCN x 10 days.¹² When an older infant or child is diagnosed, it must be determined if the disease is congenital or acquired.¹²

Social Drivers of Health and Missed Opportunities: CS is preventable but stemming its rise will not be easy. 2023 data on the mothers of the 3882 infants with congenital syphilis show only 49% of mothers had timely testing for syphilis² and only 9% of mothers had adequate treatment². These are grim statistics.² Social Drivers of Health (SDOH) and missed opportunities factor into these statistics. Access to health care is essential. All health care encounters during pregnancy serve as an opportunity to screen for syphilis, whether in emergency departments, or walk in clinics, jails, syringe service programs, maternal & child health, local screening events, homeless shelters, substance use treatment centers, etc.¹⁴ Many organizations, including IHS, have strategic plans to improve care and decrease SDOH.¹⁵

A Call to Action to reduce/eliminate Congenital Syphilis in Indian Country;

- Study syphilis, recognize the many presentations of syphilis and CS, “Know thy Enemy”.
- Consider syphilis or CS in the differential diagnosis. We must think of it to diagnose it.
- Test and treat quickly and adequately.
- Adopt the ACOG standard of testing all pregnant patients three times during pregnancy.
- For patients with fragmented care: test and treat when and wherever the patients present for care.
- Pediatric providers should know the maternal syphilis status at the first infant visit.

Findings:

Congenital syphilis is a national public health crisis. CS is preventable, treatable, and curable. Effective prevention of CS depends on screening, diagnosing and treating syphilis among pregnant persons. Evaluation, identification of infection and treatment of the infant is imperative.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

1. Leslie SW, Vaidya R. [Congenital and Maternal Syphilis](#). StatPearls. Last updated: August 17, 2024.
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3. Machevsky A, et al. [Rising stillbirth rates related to congenital syphilis in the United States from 2016 to 2022](#). *Obstetrics & Gynecology*. Oct 2024. 144(4):493-500.
4. Easterlin M, et al. [Maternal-to-fetal transmission of syphilis and congenital syphilis](#). *Neoreviews*. 2021. 22(9): e585-599.
5. Sankaran D, Partridge A, Lakshminrusimha S. [Congenital syphilis- An illustrative review](#). *Children*. 2023 Jul;10(8):1310.
6. Tudor ME, Al Aboud AM, Leslie SW, et al. [Syphilis](#). StatPearls [Internet]. Last updated: August 17, 2024.
7. Centers for Disease Control and Prevention. [Vital Signs: Missed opportunities for preventing congenital syphilis – United States, 2022](#). *MMWR*. November 17, 2023. 72(46):1269-1274.
8. American College of Obstetricians and Gynecology. [Screening for syphilis in pregnancy](#). Practice Advisory: April 2024.
9. Centers for Disease Control and Prevention. [CDC Laboratory Recommendations for Syphilis Testing, United States, 2024](#). *MMWR*. February 8, 2024. 73(1):1-32.
10. Centers for Disease Control and Prevention. [Syphilis during pregnancy](#). STI Treatment Guidelines, 2021. Last reviewed: July 22, 2021.
11. American Academy of Pediatrics. Red Book. [Book Chapter: Syphilis](#). Published 2024.
12. Centers for Disease Control and Prevention. [Congenital syphilis](#). STI Treatment Guidelines, 2021. Last reviewed: July 22, 2021.
13. Leslie SW, Vaidya R. [Congenital and Maternal Syphilis](#). StatPearls. Last updated: August 17, 2024.
14. American College of Obstetricians and Gynecology. [Screening for syphilis in pregnancy](#). Practice Advisory: April 2024.
15. Indian Health Service. National Pharmacy and Therapeutics Committee. [STI Strategic Initiative](#). Accessed Nov 2024.

****Congenital Syphilis Links****

- ❖ NPTC Strategic Initiative: <https://www.ihs.gov/nptc/strategic-initiatives/sti/>
- ❖ IHS Syphilis: <https://www.ihs.gov/sti/syphilis/>
- ❖ AAP Congenital Syphilis Diagnosis Algorithm:
 - [Red Book Interactive Algorithms | Red Book Online | American Academy of Pediatrics \(aap.org\)](#)
 - <https://pmc.ncbi.nlm.nih.gov/articles/PMC10453258/>
- ❖ Syphilis Screening and Testing: <https://www.cdc.gov/mmwr/volumes/73/rr/rr7301a1.htm>
 - <https://pmc.ncbi.nlm.nih.gov/articles/PMC4999316/table/T1/>
- ❖ CDC Treatment Guidelines:
 - CS: <https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm>
 - Pocket guide: <https://www.cdc.gov/std/syphilis/syphilis-pocket-guide-final-508.pdf>
 - Syphilis: <https://www.cdc.gov/std/treatment-guidelines/syphilis.htm>
 - Mobile app: <https://www.cdc.gov/std/treatment-guidelines/provider-resources.htm>
- ❖ Comprehensive AI/AN resource: <https://www.indiancountryecho.org/resource-hubs/syphilis-resources/>
- ❖ Congenital and Maternal Syphilis Education:
 - <https://www.ncbi.nlm.nih.gov/books/NBK537087/>
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10453258/>
 - [Congenital syphilis: Clinical manifestations, evaluation, and diagnosis – UpToDate](#)
 - <https://pmc.ncbi.nlm.nih.gov/articles/PMC10453258/>