Congenital syphilis prevention

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Congenital syphilis has been increasing at an alarming rate. Women's health nurse practitioners and other advanced practice registered nurses providing care for reproductive-age patients can help decrease the incidence of this avoidable pregnancy complication by addressing missed opportunities for prevention. This article provides practical suggestions for syphilis screening, diagnosis, and treatment that can be incorporated into practice.

KEY WORDS: congenital syphilis, prenatal care, prevention, pregnancy complication

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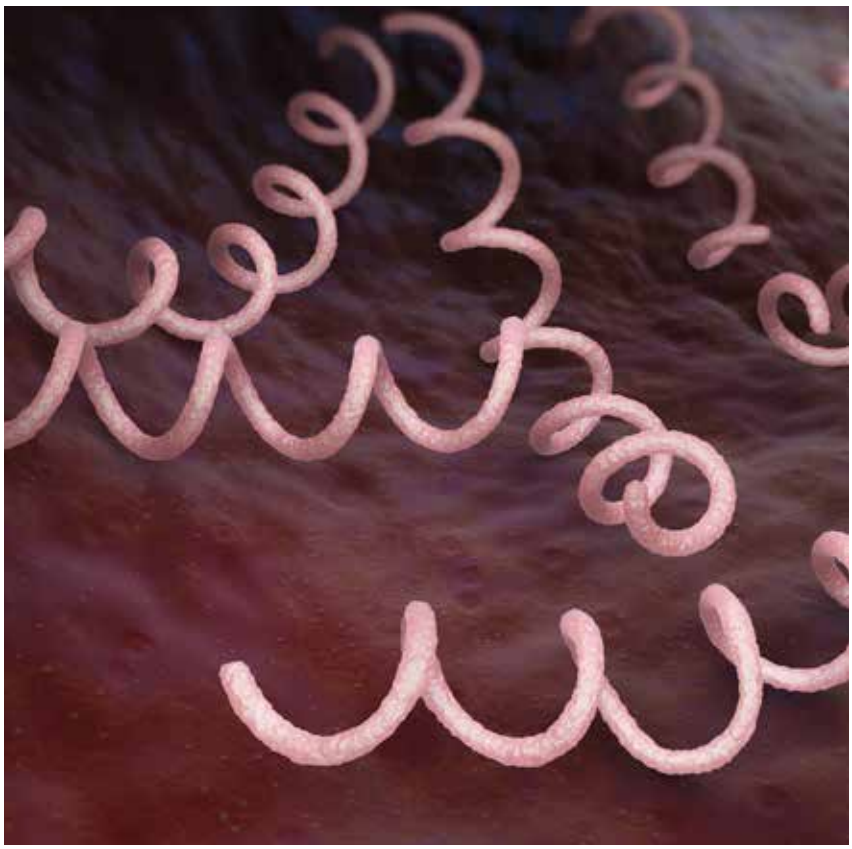

After reaching an historic low in 2000, the United States has seen an alarming increase in the number of cases of syphilis. There were 176,713 cases of syphilis (all stages) in the US in 2021, up 74% from 2017.[1] Even more concerning, the cases of congenital syphilis (CS) have increased by 203% since 2017, with 2,855 cases in 2021, including 220 deaths.[1] Congenital syphilis is preventable through the prompt identification and treatment of pregnant patients with syphilis. The Centers for Disease Control and Prevention (CDC) identified missed opportunities in a 2020 report. Awareness of these missed opportunities is essential for women's health nurse practitioners (WHNPs) and other advanced practice registered nurses (APRNs) providing reproductive and prenatal healthcare to address this problem in their own practice. This article provides a review of syphilis infection and its consequences, as well as screening, diagnosis, and treatment guidelines with a focus on the prevention of CS.

Syphilis infection and consequences

Syphilis is caused by the spirochete *Treponema pallidum*. It is transmitted via contact with a syphilis lesion, the body fluids of an infected person, or through vertical transmission from mother to fetus.[2] Signs and symptoms of infection are varied and may be missed by both patient and provider. About

3 weeks after exposure, a single, usually painless chancre will develop in the genitals or mouth at the site of exposure. This primary lesion will resolve spontaneously within 3 weeks.[3] Secondary syphilis often presents with a brownish rash on the hands/feet and lymphadenopathy approximately 2 to 6 weeks after the initial lesion resolves.

If syphilis goes untreated for several years, it proceeds to the tertiary level where gummata, cardiac, and neurologic symptoms result. Other symptoms that may be present at any stage include visual or auditory symptoms or alopecia.[3] Patients who have no symptoms but have a positive serology are in a latent phase, either early (infected < 1 year) or unknown/late.

In contrast to sexual transmission of syphilis, which is believed to only occur when mucocutaneous lesions are present, when a person with syphilis is pregnant, the infection can be transmitted at any stage to the fetus resulting in stillbirth, preterm birth, impaired growth, and placental abnormalities. Depending on the time of exposure, CS may result in bone deformities, jaundice, neurologic problems, blindness, deafness, or neonatal death.

Risk factors associated with acquiring syphilis during pregnancy include having more than one partner in the last year, previous diagnosis with a sexually transmitted infection, transactional sex, late entry into prenatal care, methamphetamine or heroin use, incarceration of the patient or partner, military service of the patient or partner, and homelessness or housing instability.[1,2,4] Higher incidence of syphilis infection in Black, Hispanic, and Native American/Pacific Islander populations has been reported. This racial and ethnic disparity is primarily due to social determinants and is not a reflection of sexual behaviors.[5] It is important to note that in a 2019 analysis of CS cases, half of the diagnosed patients had no identified risk factors.[4]

Missed opportunities to prevent congenital syphilis

In a 2018 analysis of nationally reported demographic and clinical data on mothers and infants with syphilis, four main issues were identified as missed opportunities to prevent the cases of CS.[6] These issues were: lack of timely prenatal care (PNC), lack of syphilis screening even with timely PNC, failure to treat adequately when syphilis was diagnosed, and late identification of seroconversion during the pregnancy (infection/reinfection < 30 days prior to delivery).

Lack of timely prenatal care

WHNPs and other APRNs providing care for reproductive-age persons who could become pregnant can provide patient education during wellness visits about the importance of early diagnosis of a pregnancy and early PNC when planning to continue a pregnancy. Additionally, they can consider how to mitigate barriers to PNC. This begins with listening to patients to learn what barriers may exist and to guide person-centered care. Patient-identified barriers to PNC include limited office hours, transportation problems, and lack of childcare. Language barriers or low health literacy may impact understanding of the need for or how to access PNC. Pregnant individuals who are experiencing housing instability, intimate partner violence, or alcohol/other substance misuse may be afraid to seek care due to concerns about losing their children. Importantly, some pregnant individuals have noted feeling judged or disrespected due to their circumstances resulting in negative patient–provider relationships and avoidance of PNC.[7] Bias and social and structural barriers must be identified and addressed.

Efforts to ensure that prompt prenatal care is available and accessible are essential. When a pregnant patient is not able to be seen for an initial prenatal visit in a prompt manner, screening tests could be considered prior to the visit. Additionally, healthcare providers can follow the United States Preventive Services Task Force current recommendation to screen asymptomatic, nonpregnant adolescents and adults who are at increased risk for syphilis infection as another strategy for identification and treatment of syphilis prior to a pregnancy.[5] Support to decrease rates of CS can come from APRNs working outside reproductive healthcare. Prenatal care can begin wherever a pregnant patient is seen. For example, if pregnant patients present to primary care, an STI clinic, an emergency department, urgent care, a shelter, a correctional facility, or a medication-assisted opioid use disorder (MOUD) program, a syphilis test could be ordered along with other bloodwork. Referral to PNC can be facilitated by working with a local provider.[8]

Lack of syphilis screening even with timely prenatal care

The CDC, American College of Obstetricians and Gynecologists, and American Academy of Family Physicians recommend screening all pregnant persons at the first prenatal visit.[4] Patient education on the importance of testing should be provided in a culturally and linguistically appropriate manner. Barriers to getting lab work done can be reduced by offering onsite blood draws to

Box 1. Assessment for stage of syphilis infection[2]

- History of syphilis–obtain results of previous serologic tests for comparison
- Timing of known exposure
- Signs or symptoms of syphilis in the past 12 months
  - Primary syphilis–single usually painless chancre at site of exposure
  - Secondary syphilis–lymphadenopathy that may be diffuse; nonpruritic, red or copper-colored lesions on chest, back, palms, soles; mucous patches; condylomata lata
  - Tertiary syphilis–cardiac involvement, gummatous lesions, tabes dorsalis, general paresis
  - Latent phase (early, late, unknown duration)–no signs or symptoms

send samples to the lab and by providing transportation vouchers if needed. Reassuring patients who may be using illegal substances that they will continue to receive services in a caring and respectful manner provides encouragement for testing. A "tickler" system or prompt in an electronic health record to identify patients who do not get lab work done supports outreach.

The diagnostic process for syphilis is the same for pregnant and nonpregnant patients. Syphilis screening tests are done according to the traditional algorithm or reverse algorithm. Healthcare providers should be aware of which algorithm their laboratory uses so that they can accurately interpret results. In the traditional sequence, a nontreponemal test such as rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) is done. If the nontreponemal test is negative, it is unlikely the patient has syphilis. However, because these tests may be negative in very early primary syphilis, if infection is strongly suspected, it should be repeated in a month.[2] If the nontreponemal test is positive, a confirmatory treponemal test is done, such as the *T. pallidum* passive particle assay (TP-PA), and a quantitative nontreponemal test is reported as a dilution titer, such as 1:8. In the reverse sequence, an automated treponemal immunoassay, such as an enzyme immunoassay (EIA), identifies antibodies. If this test is reactive, it indicates the person has syphilis, has had syphilis in the past, or may not have been fully treated. A reactive EIA is followed by a quantitative nontreponemal test and TP-PA for confirmation.[2] In screening and testing for response to treatment, the same type of nontreponemal test (RPR or VDRL) should be used as quantitative results from the two tests cannot be compared directly with each other.[2]

Failure to adequately treat syphilis once diagnosed

Treating syphilis during pregnancy requires collaboration with the local health department, maternal-fetal medicine practitioner, and/or infectious disease specialist to facilitate appropriate and effective management. The earlier the treatment, the better the fetal outcomes. Treatment of the mother during the last month of pregnancy or with a drug other than penicillin is not considered adequate treatment for the fetus.[2] Unless there is medical documentation of prior diagnosis with adequate treatment and with titers that have declined appropriately, positive results indicate a need for treatment.[2] Treatment is based on stage. The stage is determined through lab test interpretation (positive RPR and positive TP-PA), a thorough history, and a physical exam. Components of the history and physical exam are listed in *Box 1*.

The recommended treatment for all stages of syphilis is parenteral penicillin G benzathine 2.4 million units. No other penicillin formulations should be used as these have not been shown to be effective. For early syphilis of less than 1 year duration, one dose is given. Fetal ultrasound should be ordered for patients diagnosed after 20 weeks.[2] A second dose 1 week after the initial dose is beneficial for fetal treatment when a pregnant patient is in the early stages of syphilis if fetal ultrasound findings suggest CS.[2] Treatment of latent/unknown duration and tertiary syphilis requires three doses, each 1 week apart. The weekly three doses over a period of 3 weeks are needed because the organism divides more slowly in later stages of the infection. The importance of adhering to this regimen to benefit both patient and fetus should be stressed. Due to physiologic changes in pregnancy increasing drug elimination, pregnant persons with latent/unknown duration should restart the series if subsequent doses are not given by day 9.[2] Efforts should be made to contact patients who have not come in by day 7 and to facilitate getting their next dose by day 9.[2] Doxycycline, the alternate treatment, is not given to pregnant persons due to fetal effects. Pregnant persons who are allergic to penicillin should be desensitized and treated.[2] Skin testing to confirm penicillin allergy and desensitization should be done in consultation with an allergy specialist.

Partner testing and treatment, along with abstinence until treatment is completed, is essential. Attention to eliminating or decreasing risk behaviors can reduce the potential for reinfection.

Jarisch-Herxheimer reaction can occur as a reaction to the treatment and is not an allergic reaction to penicillin. Symptoms include a fever, chills, tachycardia, headache, and

Box 2. Learning resources on syphilis diagnosis and management

National STD Curriculum (uw.edu)[A] free online modules and podcasts
Home | National Network of STD Prevention Training Centers (nnptc.org)[B] self-study modules and live event information
Home - CDC TRAIN[C] - an affiliate of the TRAIN Learning Network powered by the Public Health Foundation August 2023 module on congenital syphilis
Recommendation: Syphilis Infection in Pregnant Women: Screening | United States Preventive Services Taskforce (uspreventiveservicestaskforce.org[D]) undergoing update 2023

Box 3. State prevalence and syphilis screening mandate resources

Table 13. Primary and Secondary Syphilis — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2021 (cdc.gov) https://www.cdc.gov/std/statistics/2021/tables/13.htm[E]
Table 20. Congenital Syphilis — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2021 (cdc.gov) https://www.cdc.gov/std/statistics/2021/tables/20.htm[F]
Prenatal Syphilis Screening Laws (cdc.gov) https://www.cdc.gov/std/treatment/syphilis-screenings.htm[G]

body aches. The reaction may begin 2 to 8 hours after the injection and lasts about 24 hours.[2] Treatment is supportive to manage symptoms. This reaction is more common when the titers are higher due to the rapid destruction of spirochetes.[2] The destruction causes a release of prostaglandins and cytokines, increasing the risk for preterm labor, fetal heart rate changes, such as decelerations or tachycardia, or decreased fetal movement in patients greater than 20 weeks' gestation.[3] The concern of a Jarisch-Herxheimer reaction should not delay treatment. Medication can be administered in a labor and delivery unit to monitor any reaction if this is a concern. At a minimum, patients need to be instructed to contact the healthcare provider if they notice any fever, contractions, or decrease in fetal movement.

Follow-up with serial nontreponemal titers is needed post treatment. In pregnant persons treated prior to 24 weeks' gestation, waiting 8 weeks to repeat the nontreponemal titer is recommended.[2] A titer should be drawn at delivery. Generally, a fourfold decline in the nontreponemal titer is evidence of successful treatment. However, this can take up to 1 year or more depending on the stage, so it is unlikely to occur during the pregnancy.[2] If there is concern of reinfection, titers can be repeated anytime. Indications of reinfection include signs or symptoms that recur, new signs or symptoms attributable to primary or secondary syphilis, or a sustained fourfold or greater increase in the nontreponemal titer that persists for longer than 2 weeks.[2] See *Box 2* for learning resources on syphilis diagnosis and management.

Late identification of seroconversion

Screening for syphilis should be repeated at 28 weeks and at delivery, depending on assessment of risk. Risk assessment should consider prevalence in the community served. State and local health department web pages can help identify the risk level in a community. This can vary greatly. For example, 2021 data showed 232.3 cases of CS per 100,000 in Arizona while Maine, New Hampshire, and Wyoming had no cases.[1] Some states mandate third-trimester and delivery screenings. See *Box 3* for links to view state-specific prevalence rates and prenatal syphilis screening laws.

Testing for syphilis should be done when there are abnormal fetal ultrasound findings such as hepatomegaly, placentomegaly, hydramnios, ascites, or fetal hydrops that could indicate CS and when there is fetal loss after 20 weeks' gestation.[2,3] It is important to be aware of possible signs and symptoms of syphilis and provide testing whenever these are present in a pregnant patient. Treatment of the partner at the initial diagnosis of the patient is essential to avoid reinfection. If the partner tests positive at any time, the patient should be treated promptly.[2]

Conclusion

Congenital syphilis has been increasing at an alarming rate. Women's health nurse practitioners and other APRNs providing care for reproductive-age patients can help decrease the incidence of this highly preventable pregnancy complication by addressing missed opportunities identified in the literature. Prevention of syphilis in pregnant individuals is supported by screening childbearing-capable persons. Assuring timely prenatal care enables early syphilis screening. Ongoing evaluation for risk factors can prompt rescreening to identify infections acquired during the pregnancy. Facilitating timely and appropriate treatment and follow-up for patients diagnosed with syphilis may prevent the development of CS in the fetus. Preventing CS requires all healthcare providers to remain alert to syphilis prevalence in their

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The exact etiology of the vaginal dysbiosis is unknown. The vaginal microbiome in reproductive-age women is a complex balance of pH, lactobacilli, and hormonal levels dominated by estrogen, with transient fluctuations dependent on sexual activity, menses, and personal hygiene practices.

Table 2. Treatment of desquamative inflammatory vaginitis[5]

Clindamycin	Clindamycin 2% cream 5 g vaginally daily at bedtime for 2–4 weeks; consider maintenance therapy twice a week for 2–6 months.
	Clindamycin 100 mg suppository Two suppositories vaginally daily at bedtime for 2–4 weeks; consider maintenance therapy twice a week for 2–6 months.
Corticosteroids	Hydrocortisone 300–500 mg vaginally daily at bedtime for 2–4 weeks; consider maintenance therapy twice a week for 2–6 months.
	Cortisone acetate suppository 25 mg vaginally daily at bedtime for 2–4 weeks; consider maintenance therapy twice a week for 2–6 months.

DIV is a noncommunicable inflammatory process and is a diagnosis of exclusion. It can be challenging to diagnose because of lack of healthcare provider awareness, similarities in clinical presentation to other causes of vaginitis, and lack of definitive tests. As healthcare provider knowledge and appropriate diagnosis of DIV are low, accurate reporting of incidence and prevalence are lacking, although these are believed to range from 0.8% to 4.3%.[2]

Diagnosis and treatment

Diagnosis of DIV is indicated by vaginal inflammation marked by spotted ecchymosis or petechiae, erythema, focal or linear erosions, and at least one of these patient-reported symptoms: vaginal discharge, dyspareunia, pruritus, burning, and irritation; a pH greater than 4.5; microscopy of vaginal flora containing an increased number of parabasal and inflammatory cells and a leukocyte-to-epithelial ratio greater than 1:1; and exclusion of BV, trichomoniasis, and candidiasis (*Table 1*).[1] Gonorrhea, chlamydia, atrophic vaginitis, and use of vaginal irritants should also be excluded.

Clindamycin and hydrocortisone are the recommended treatments for DIV. Because DIV can recur, maintenance therapy may be indicated (*Table 2*).[5] Data on the use of clindamycin in all trimesters of pregnancy and during breastfeeding are reassuringly safe.

SW was treated with a 2-week course of nightly 2% vaginal clindamycin cream and nightly vaginal hydrocortisone cream 500 mg. She was encouraged to continue her already established vaginal hygiene practices and advised to return if symptoms recur. She restarted her combination oral contraceptives. Symptoms resolved with treatment, and the patient was not seen again in the clinic until her next annual exam.

Conclusion

Desquamative inflammatory vaginitis falls under the umbrella of chronic vaginitis. Chronic vaginitis is characterized by prolonged and recurrent inflammation or infection of the vagina. The term is not a true diagnosis but rather an array of symptoms encompassing vulvovaginal itching, burning, irritation, dyspareunia, and abnormal vaginal odor or discharge. Chronic vaginal symptoms are a frequent reason for women to visit their healthcare provider. When an accurate diagnosis is not made and appropriate treatment is not initiated in a timely manner, additional sequelae such as chronic pain, discomfort with self or others, periods of absence from school or work, and withdrawal from social spheres can occur.[6]

DIV is not a common cause of inflammatory vaginal symptoms. When patients present with symptoms of vaginitis, it is appropriate for the workup to include common etiologies such as candidiasis, trichomoniasis, chlamydia, gonorrhea, and vaginal atrophy. However, when these diagnoses are excluded or for patients presenting with recurrent or persistent symptoms of vaginal discharge, pruritus, burning, irritation, and dyspareunia who have not respond-

ed to treatment, providers should be cognizant of other less common causes including DIV. Early diagnosis and treatment can significantly improve patients' overall quality of life by decreasing pain and improving sexual health. ■

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communities and follow best practices in prevention. APRNs can be powerful advocates for state policies requiring serial syphilis screenings in pregnancy to influence provider practice.[9] Participation on facility, local, or state CS case review boards provides an opportunity to contribute to identifying barriers to care and targeted interventions. ■

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Web resources

A. std.uw.edu/
B. nnptc.org/
C. train.org/cdctrain/home
D. uspreventiveservicestaskforce.org/uspstf/recommendation/syphilis-infection-in-pregnancy-screening
E. cdc.gov/std/statistics/2021/tables/13.htm
F. cdc.gov/std/statistics/2021/tables/20.htm
G. cdc.gov/std/treatment/syphilis-screenings.htm