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SEXUAL HEALTH ECHO: SYPHILIS IN PREGNANCY AND CONGENITAL SYPHILIS

Tieg Beazer, DO, MS

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[video transcript]

00:08
And with that, I'll hand it over to Dr. Beazer. Thank you. Thank you again for having me. Good afternoon everyone. Again, my name is Tieg Beazer. I am currently one of the second year maternal fetal medicine fellows at the University of Rochester. This, presentation on syphilis and pregnancy and congenital syphilis was constructed under the guidance of my mentors, doctors coordinate with Olson-Chen and Dr. Ponnila Marinescu, who are both part of the Maternal Fetal Medicine faculty here. I do not have any disclosures. Here are the objectives of today's presentation. One review the epidemiologic trends of syphilis in the general population and pregnant people, as well as the increasing prevalence of congenital syphilis, to discuss the clinical presentation of each stage of syphilis infection, three review laboratory screening and confirmatory testing for syphilis. Four, discuss the unique treatment guidelines for syphilis diagnosed in pregnancy. And five learn about the fetal ultrasound findings and physical manifestations associated with congenital syphilis. So Syphilis is a systemic infection caused by a gram negative spirit keep bacteria called Treponema pallidum , the spirochaete enters the body through traumatized epithelium during sexual contact with an infectious lesion.

01:45
In 2020, 133,945, cases of syphilis were reported in the United States, about 31% of those cases reported were a primary and secondary syphilis, the most infectious stages of the disease. Rates of primary and secondary syphilis are traditionally lower amongst women. However, rates of syphilis amongst women have increased substantially in recent years, which is believed to be related to the increasing rate of substance abuse. This is a graph of the reported cases of syphilis diagnosed in pregnant people and the reported cases of congenital syphilis. As you can see, syphilis and pregnancy and congenital syphilis are steadily on the rise.

02:40
During 2012, to 2019, congenital syphilis rates in the United States increased from 8.4 to 48.5 cases per 100,000 births. That's a 477.4% increase. Similar to the nation of white trend cases of early syphilis and congenital syphilis are increasing in New York state. On the left side of this table, is a list of some of the counties in New York State and the number of early syphilis diagnoses from 2018 to 2021. And on the right side of this table is the total number of congenital syphilis diagnoses listed in descending order. University of Rochester where I'm currently an MFM fellow is located in Monroe County, which has the second highest number of early syphilis and congenital syphilis diagnoses in the state.

03:38
At least 45 states have prenatal syphilis testing requirements with high variability among those requirements. New York State Public Health law mandates syphilis screening of pregnant persons at the time of diagnosis in pregnancy, and again upon delivery. third trimester syphilis screening at 28 weeks for all pregnant persons, or as soon as reasonably possible but no later than 32 weeks of pregnancy is highly recommended to avert congenital syphilis in New York

State. In 2019, the New York State Department of Health began mandating syphilis screening at 28 weeks. Providers are encouraged to pair third trimester syphilis screening with the strongly recommended third trimester HIV screening. Any woman who has a stillborn fetus after 28 Sorry, excuse me after 20 weeks gestational age, must be tested for syphilis, which was a recommendation by the New York State and American College of Obstetrics and Gynecology guidelines.

04:50
Next, we will discuss the clinical presentation of syphilis by stage. The primary stage occurs approximately 10 days to three months post exposure and consists of a shaker which is an isolated nontender ulcer with raised rounded borders. shrinkers are often found on the cervix, vagina, vulva, mouth or anus. The secondary stage of syphilis occurs typically between six weeks to six months push anchor, and consists of a maculopapular rash all over the entire body, palms, soles and mucous membrane. Secondary syphilis can also manifest as a Condylomata lata fever, malaise and less commonly cranial nerve dysfunction, meningitis, Hepatitis and arthritis. From left to right here, you will see a cannula condyloma Lata on the external genitalia of a female, and then the maculopapular rash it's discussed before on the hands and then over all over the body. So early late, and Syphilis is diagnosed within one year of infection and can occur with secondary signs and symptoms. Lately insists illness is diagnosed greater than one year after the initial infection. Then tertiary syphilis occurs with untreated syphilis that can appear about 20 years after latency and manifests within the cardiovascular system, central nervous system or there can be musculoskeletal involvement as well. I would like to incorporate a recent outpatient consultation I received as we discussed the recommended testing treatment and follow up for syphilis diagnosed in pregnancy. So patient CS is a 29 year old in our first pregnancy at 13 weeks, five days with a positive RPR in her initial routine prenatal labs. Here's a diagram outlining the traditional screening screening route algorithm. Non treponemal tests are nonspecific screening tests which are traditionally used for initial syphilis screening due to their low costs, ease of performance and ability to be quantified to determine response to therapy. A positive non treponemal Test Results should prompt clinical assessment and confirmation with a trip and email specific tests such as the fluorescent treponemal antibody absorption, or treponema pallidum particle agglutination. As false positive non treponemal tests can be caused by recent vaccination, febrile illness, IV, substance abuse and lupus. It is important to note the species specific treponemal tests typically remain positive for life following infection, whereas a positive non treponemal test after treatment can indicate a new infection, evolving response to recent treatment or treatment failure. Non treponemal tests are the RPR and vdrl or semi quantitative, positive non treponemal tests are reported as a tighter the tighter represents the amount of antibody present IgM and IgG. And the activity of the infection titers are followed after treatment to determine a response therapy or response to therapy Excuse me. So back to our patient, she had the positive RPR. In her initial routine prenatal labs, her confirmatory test was positive and our RPR titer was initially one to 128. Reporting a new positive prenatal or delivery syphilis result is mandatory. Physician physicians, nurses, laboratory directors infection control practitioners, healthcare facilities, state institutions and schools are eligible reporters. Positive syphilis results should be reported to the patient's local health department where they reside, which will require submission of a confidential case report form the DL H 389. The state or local health department can assist in following up with

patients and their partners to ensure access to treatment and further care. Once a diagnosis of Syphilis is confirmed, it is important to test the patient for other STIs including HIV, Hepatitis B and or C. Gonorrhea and also chlamydia. For the CDC. All women who have syphilis should be offered HIV testing at the time of diagnosis.

09:54
long acting benzathine penicillin also known as penicillin G is the first lie An antibiotic for syphilis infection. I would like to emphasize that Ben's Ben's have been penicillin G should not be confused with procaine penicillin g. in non pregnant patients who are penicillin allergic doxycycline can be used as an alternative to treat syphilis. However impatient in pregnant patients penicillin G is the only known effective antimicrobial for treating fetal infection and preventing congenital syphilis. Therefore, if a pregnant patient is allergic to penicillins, they will need D sensitization in order to receive treatment for their syphilis infection. So back to her patient, who had the positive RPR. Her confirmatory test was positive and her RPR titer was one to 128. She reports that she had a rash on her abdomen, hands and arms not involving the palms and soles approximately eight months prior, which was attributed at that time to an allergic reaction to an oral contraceptive pill. Her last negative document syphilis screening tests was in 2017. So based off of this information, she was determined to have early latent syphilis. primary secondary and early late and syphilis requires one I am dose events have been penicillin G 2.4 million units. There is evidence that an additional dose of penicillin G 2.4 million units I am one week after the initial dose can be beneficial in pregnant patients with primary secondary or early late and syphilis to prevent congenital syphilis. Late Late in or tertiary syphilis requires three doses of penicillin. 2.4 million units, I am weekly for three doses. More than nine days between doses is not acceptable for pregnant women receiving therapy for lately and syphilis, as the optimal interval between doses is seven days for pregnant women. The pregnant woman does not return for the next dose on day seven. Every effort should be made to contact her and link her to immediate treatment within two days to avoid retreatment. It is hard to adequately treat syphilis and prevent congenital syphilis that the patient delivers within 30 days of diagnosis and or treatment. nonpregnant patients can receive doxycycline 100 milligrams PLB a day for 14 days with primary secondary or early latent syphilis whereas late latent, or tertiary syphilis infection would require doxycycline 100 milligrams B VDPAU for four weeks.

13:07
Of the Gerrish Herxheimer reaction is an acute, febrile self limited reaction that occurs within 24 hours of antibiotic treatment for a spirit of key infection. It occurs in approximately 10 to 35% of cases, most commonly after treatment of early syphilis, likely because the bacterial loads are higher during the stage of infection. Symptoms include fevers, chills, riders, myalgias, nausea, vomiting, headache, tachycardia, hypotension, hyperventilation, flushing diaphoresis, and exacerbation of a rashes if it is initially present at the time of treatment. It is important to remember to counsel patients this is a reaction to the infection and not an allergic reaction to penicillin. The Gerrish Herxheimer reaction may induce early labor or caused fetal distraction in pregnant women. So pregnant people should be advised to seek obstetric attention after treatment if they noticed a fever contractions or a decrease in fetal movement. There is no data

to support treatment with steroids to prevent this reaction. I would like to emphasize that the risk of a Jerash Herxheimer reaction should not prevent or delay therapy in pregnant women.

14:37
After treatment, it is recommended to follow the non treponemal titers. We typically measure titers in the third trimester and at delivery but it should be a minimum of eight weeks after treatment. Non treponemal titers can increase immediately after treatment presumably related to their treatment response. Therefore, unless symptoms and signs exist apart, primary or secondary syphilis, a follow up titer should not be repeated until approximately eight weeks after treatment. A fourfold decrease in titers. After treatment is a clinically significant response which is expected by six months post treatment. It is recommended to repeat treatment if titers increase or do not fall appropriately. Back to our patients Yes, with the initial titer of one to 128 she received one dose of penicillin and anatomy ultrasound performed at 20 weeks, five days to know gross fetal anomalies. And a repeat titer. Three months later was one to 32 on her third trimester labs. We are currently awaiting repeat data at the time of her delivery which was six which will be six months after her initial treatment.

15:58
So Miss doses greater than nine days between doses for treatment of lately and syphilis require repetition of the full course of therapy, which I had mentioned earlier. And patients with a history of treated syphilis, a positive non triple normal test or PRP or vdrl. Often indicates a new infection and involving response to recent treatment or treatment failure. A fourfold rise in a non treponemal titer sustained for two weeks, or six months after treatment can represent treatment failure. Pregnancy can elevate titers, so it may be difficult to properly identify failed treatment or reinfection in pregnancy. I will now review the pathogenesis and clinical manifestation of congenital syphilis. Sphere kids readily cross the placenta and can access a fetus as early as nine to 10 weeks gestational age, infection begins in the placenta, the placenta becomes thickened Dennett Dimittis, then the amniotic fluid becomes infected, hematologic abnormalities can develop which can then lead to ascites and nonimmune hydrops. The syphilis triad includes large hypercellular villi, proliferative vascular changes, and acute or chronic the latest. The frequency of vertical transmission increases with gestational age, but the severity of fetal infection decreases later in pregnancy. Early stages of syphilis are associated with an increased risk of vertical transmission. So early, early syphilis can carry a 40 to five 50% risk of congenital syphilis, whereas late stuff like lately and syphilis, excuse me carries a 10% risk of congenital syphilis.

18:03
congenital syphilis can cause an obliterative and arthritis involving many organs including the liver, kidneys, pancreas, spleen, bone, lungs, heart and the brain, vibrant fibrosis and Goombas are frequently noted and congenitally infected tissues. sonographic evidence of syphilis infection is associated with an increased risk of having signs of congenital syphilis at delivery. hepatic megali is one of the most sensitive findings it's a reliable sign correlated with detection of trapped means in that amniotic fluid. So here you will see the This is a picture of the fetal chest. The ribs are seeing here, the rest of the abdomen is flow here in the bottom half of the fetus. This is highlighting and a large liver spanning the width of this fetus. hydrops fatalis is another

manifestation of fetal infection with syphilis. And it occurs when an abnormal amount of Sadie's occurs in two or more body cavities of a fetus. Placental megali is described as the width of the placenta measuring greater than four centimeters in diameter. This fetuses placenta measures approximately seven centimeters in diameter seen here. And then, dilation of the small bowel can also occur. So, to diagnose infection of fetal syphilis can be performed with a courtesan thesis or or percutaneous umbilical blood sampling, which is a diagnostic prenatal test in which a sample of the baby's blood is removed from the umbilical cord for testing. It can detect IgM antibodies and fetal circulation. an amniocentesis seen on the right side of the screen involves the removal and testing of a small sample of cells from amniotic fluid. A PCR detecting treponema pallidum DNA or darkfield examination on amniotic fluid can be performed to diagnose fetal syphilis. Early manifestations of congenital syphilis are defined as characteristics that occur before two years of age and includes the following diffuse macular rash, rhinitis, and I just wanted to highlight here, although this picture is an of an older individual congenital syphilis infection can cause purulent or hemorrhagic nasal discharge which can lead to ulceration at the filth room. vestibule and nasal tip with just with destruction of the nasal septum seen in the picture here hepatocyte vanilla Splinter mega li can also occur anemia, jaundice, pneumonia, or myocarditis. Late manifestations of congenital syphilis are defined as characteristics that occur after two years of age if syphilis remains untreated. So that can include the Hutchinson's triad, which involves interstitial keratitis or pain tearing or blurred vision. Dental abnormalities seen here with Hudgins hips T, and CNS involvement, so hydrocephalus, seizures and cognitive delay.

21:54
So here are a summary of maternal fetal medicine recommendations at the time of diagnosis. So it's our goal to make sure the infection was reported to the local health department to also test the patient for other STIs obtain a detailed anatomic ultrasound between 18 to 20 weeks gestational age are at the time of diagnosis in the third trimester. Repeat titers at a minimum of three months after diagnosis and or at the time of delivery, and confirmed treatment response versus failure with repeat titers six months after diagnosis.

22:37
The following signs are clinical scenarios involving diagnosis of syphilis and pregnancy and congenital syphilis and ultrasound. Then I was asked to comment on from the Maternal Fetal Medicine perspective. So what is our management of patients who have ongoing risk factors for contracting syphilis? It's important to identify risk factors within each patient so such as living in a high prevalence area, active substance abuse STIs during pregnancy, more than one or new sexual partner engaging in transactional sex, incarceration or a partner who is incarcerated, and patients who are homeless or have unstable housing. The University of Rochester is located in a high prevalence area. Therefore, we perform RPR tests in the first and third trimester of pregnancy and upon presentation for delivery. It is considered standard of care to obtain an anatomic ultrasound around 18 to 20 weeks gestational age, which can detect signs of fetal syphilis. There can be consideration for more frequent testing and those who are at higher risk, but this has worked pretty well for our institution thus far. Have you ever seen a Jarisch Herxheimer reaction actually precipitate labor. So although myself nor my mentors have seen this reaction and precipitate labor, it can occur in 10 to 35% of cases. I want to stress that the

risk of labor due to this reaction should not delay treatment. There is literature that supports consideration for administering the first dose of penicillin on a labor and delivery unit, with continuous fetal monitoring for at least 24 hours and pregnancies that have reached a gestational age when intervention would be considered. If primary or secondary stage of syphilis when the Jarisch Herxheimer reaction is more likely to occur in patients with a history of preterm birth. In turn, patients who are close to delivery, if contractions were to occur, occur, or in cases of sonographic evidence of congenital syphilis In the role of pre medication with corticosteroids or TNF alpha has been used to prevent this reaction, but it's not rarely used and there is no data in pregnant people. Most importantly, if penicillin is administered in the outpatient setting, it's important that patients receive counseling to report symptoms of labor, or decreased fetal activity to their provider immediately if it occurs after treatment. Would we ever consider inducing labor to treat a baby with evidence of congenital syphilis on ultrasound? So typical management would emphasize treatment of the infection rather than delivery as that has the potential to improve or reverse signs of fetal syphilis. However, delivery could be considered with evidence of fetal compromise, such as worsening hydrops, unrelieved with therapy or non reassuring antenatal fetal testing. But again, our goal is to adequately treat the patient and monitor for signs of fetal compromised prior to moving towards delivery. Lastly, do we routinely get referrals of pregnant patients with syphilis from smaller centers? Or is that only done if there are evident if there is evidence of anomalies on ultrasound? So as MFMs we usually receive consultations for women diagnosed with syphilis and pregnancy to provide information about the infection and perform a diagnostic ultrasound to look for signs of fetal syphilis. However, the patient then returned to their primary OBGYN provider for continued prenatal care throughout their pregnancy. They may check back in with us later in their pregnancy or postpartum to ensure their titers responded appropriately to treatment. transfers into our high risk pregnancy practice are typically for patients with medical comorbidities unrelated to their syphilis infection, or if their primary OBGYN provider is unfamiliar with managing the treatment of syphilis. We would recommend delivery at a regional perinatal center with a higher level NICU in a fetus with evidence of fetal syphilis on ultrasound. So this concludes my presentation on syphilis and pregnancy and congenital syphilis. Here is a list of my references.

[End Transcript]