Syphilis and Congenital Syphilis Transcript

DEMYSTIFYING HIV/STI TESTING, TREATMENT, AND PREVENTION WEBINAR SERIES

All right. Hi everybody. Thanks for joining. We are going to give it just another minute or so to allow people to join. OK, I see that we're starting to get there on folks joining. We do have an action-packed session for you today, so I think in the interest of time we will get started.

Good afternoon, everyone. I'm Beth Gyllstrom from the Minnesota Department of Health and I'm pleased to welcome you to the first in our three-part series: Demystifying HIV/STI Testing, Treatment, and Prevention, which we're hosting in collaboration with the Minnesota Medical Association.

So, a few quick housekeeping items. We are recording this session and then if you could please hold your questions until the end. You can also put your questions in the Q&A and if we can address them during the session, we will. We'll compile the Q&A and send it out after the webinar, as well as post it on our website and then we will post the evaluation link towards the end of the presentation and also follow up with that for registered participants. So, with all that, it's my pleasure to introduce our speaker today, Dr. Nick Lehnertz.

Dr. Lehnertz is a physician and medical epidemiologist specializing in infectious disease epidemiology, prevention, and control here at the Minnesota Department of Health. His work includes responding to novel and emerging infectious outbreaks such as SARS CoV-2 and Mpox, creating strategies to reduce risk of acquiring syphilis and HIV, and understanding the drivers and barriers to healthcare utilization, especially among disproportionately impacted populations. So, with that, I'm gonna turn it over to Dr. Lehnertz.

Thanks, Beth. And I'm gonna turn my camera off just to say bandwidth and just get rolling here because I will be honest with you, I have way too many slides and so please feel free to pop questions in the Q&A and as Beth said, we will get to them.

So, let's start off with the case. I call this mysterious case number one. All right, let's go. So, we have a 68-year-old female with a past medical history of Type-2 diabetes, hypertension, hyperlipidemia. She's got a history of Crohn's, but she's not on any immunomodulating meds, and she shows up to the clinic with a rash on her torso in her arms. She's weak. She got joint pains. She's got a sore throat. They work her up and nothing real specific, so they think that's probably a viral process. And so however? Her weakness progresses to the point where she requires a walker now and she's got blurry vision in her right eye. She sees ophthalmology that she's got some iritis and optic disc edema. During this time, she has repeated trips to the Ed for continued weakness. She develops confusion to the point where she needs to move in with her son. They do a brain MRI. Nothing remarkable there. Rheumatology rules out temporal arteritis and PMR. They gave her some steroids, but again, we really don't have a diagnosis yet and this has been going on now for four months. And again, this is a 68-year-old female with typical past medical history.

Over the next four months, she has ongoing confusion. Weakness. And now she's got vision changes and both of her eyes. She's been seeing ophthalmology and PCP multiple times. She

goes to the E.D. again, and now her rash and pharyngitis have returned. So, what are we thinking, right? Well, the PCP then sends treponemal screening and it comes back positive, which is not surprising since this is a syphilis talk. But she's positive and she has an RPR. A non-treponemal test with a titer of 1 to 4096. So she is immediately transferred to the to the metro area. She's diagnosed with anterior uveitis with ocular syphilis. She's got patchy alopecia and plantar rash, which we will learn later, are signs of secondary syphilis. She receives 14 days of penicillin G through IV and her sexual partner also tests positive for syphilis and was appropriately treated.

So in summary, we have a gazillion emergency care and hospital and primary care visits. Numerous labs, she's had an MRI, she had a biopsy. Eight months of symptoms prior to diagnostic testing and definitive treatment. The point of all of this is: think syphilis. Syphilis, as we all learned in medical school or, you know, like whatever training we received, it's the Great Pretender. It can appear like anything so constantly: think syphilis. That's the overarching point of this talk, and so big thanks to Doctor Alice Lehman for the case.

There's the title slide. This has been planned in accordance with all this stuff. So it's eligible for CME credits, and I think you're going to get a link to that at the end.

Disclosures: I have no disclosures or conflicts of interest and very importantly, the opinions that I may express during this webinar are mine and mine alone, and don't necessarily represent those of MDH or the Minnesota Medical Association.

And then I just want to point out that this work is funded by the CDC STD PCHD grant, and so during this talk, we will identify individuals as men or women in this presentation. And then here are some acknowledgements. Couldn't have done this alone.

So, I want to start with key takeaways, and I want you to if there's one slide that I want you to walk away with, it's this one, right? This sort of summarizes everything we're going to talk about in the next hour.

Syphilis rates in Minnesota and throughout the country continue to be elevated and cases occur throughout all of Minnesota. It's not just a metro sort of issue. It's not just certain populations. It's all throughout Minnesota and it's within all demographic populations, especially impacting women of childbearing age, and then of course, having a disproportionate impact on certain racial and ethnic populations. We recommend screening all individuals between the ages of 18 and 49 at least once, right? Everybody, right? And then more often, if risk factors are present and -- you can do less under 18 or over 49 as well if you know if there's new sexual initiation or new sex partners or symptoms, or even if they request it. And so, the takeaway is screen, right? You need to screen pregnant people three times during pregnancy at their first prenatal visit, again at 28 to 32 weeks, and again at delivery three times. All pregnant people.

Complicated or neuro syphilis that that infects the CNS can occur at any stage of syphilis and it's estimated that up to 40% of syphilis cases will have neurological involvement. And at some point, 40% will have neurological involvement. That's important because the treatment regimen for complicated syphilis neurological syphilis is different.

We have data that strongly supports use of doxy PEP, or post-exposure prophylaxis, with a single dose of doxycycline as a preventive strategy to decrease the incidence of syphilis and other STI's, and we'll get to that. That's important. And then syphilis, as I showed you earlier, can mimic many diseases and testing results can be difficult to interpret, so always think syphilis and if you need to, you can always reach out to MDH or your colleagues to further work this up.

What are we talking about? Syphilis is caused by the sexually transmitted infection by the bacterial troponinopalidine. This is what causes syphilis right there. You can see that Corkscrew shape you get infection through breaches in the skin or mucus membranes. It's most infectious during symptomatic early syphilis, and we'll talk about all the stages in a little bit and it's most infectious through this high burden of spirochetes actually in the lesions and these are in the shankers in the mucous patches in the condyloma lata that we oftentimes see in primary and secondary syphilis and then persons at risk of syphilis due to this breach in the skin or mucous membrane are also at increased risk for HIV.

Through that process of transmission through that broken skin, as I mentioned, is often called the Great Pretender. It can look like pretty much everything, and because it is a sexually transmitted infection, we have to put it all in the framework of stigma, right? And so, like everything we're talking about, everything from diagnosing, treatment, screening, all that kind of stuff, we have to put it in that framework of stigma. A clinical understanding and diagnosis requires a current and historical sexual history, a complete physical exam right, and to do that you have to have a trusted relationship with your patient. And so, this whole thing all goes together: trust and being able to talk to your patients authentically about their sexual behaviors, both current and past, without having that stigma around, so just keep that in mind.

Now the good stuff: syphilis can be treated with penicillin, right? You get a shot of three or even four for complicated syphilis. It can even be treated with doxycycline. This is not a complex organism to actually treat. However, the not so good is that the signs and symptoms of syphilis are transitory and can be nonspecific. You have an extended latent phase of disease, so individuals may not even recognize they are infected, right? Clinicians may not recognize that their patient is infected. Neurological manifestations, as we mentioned before, up to 40% of cases. And untreated syphilis can result in very severe sequelae and death and untreated infection during pregnancy can result in congenital syphilis.

This one is true. Interpreting testing results can be complicated, can be very complicated, right? First, if you can't culture this organism, the test requires a vena puncture, unless you're doing a rapid fingerprint testing strategy with nonconfirmatory testing for just using that and then and then presumptively treating. There are two different diagnostic algorithms. You have a traditional one and then a reverse one.

False positives can occur with non-treponemal test. You can have lots of conditions that will turn that non-treponemal needle test positive. Things like immunizations and pregnancy and IV, drug use and autoimmune conditions, all sorts of things you need confirmatory testing and titers. So, patients may have to return and positive treponemal tests remain positive after treatment, so once infected, tests will always remain positive, so there's lots of difficulty when it comes to actually diagnosing syphilis.

So, what do we care? Let's talk about the EPI for a little bit. So, this is a graph over time and I'm spreading my hands in part you can't see that. But from 1936 until 2024 and the Green Line, the green horizontal line right above 1500 cases is that 1940s baseline. That's where we were in the 1940s, and you can see from the 1950s all the way through about you know 2015 or so. We were a pretty low threshold. Under 500 cases per year total in Minnesota and then right around 2013 or 2015, we started seeing this really startling increase in the number of cases to where we are right now. We're at the 1940s level. We haven't seen this kind of syphilis activity since the 1940s. And then I put these little squares that emphasize we were down here. That's where we should be, and we're all the way up there.

I want to talk about syphilis rates by stage. We can see here that the overall syphilis rate right here 25.9 per 100,000 people, that's a 115% increase from a decade ago. OK, 2015. It was 12, and so literally over 100% increase from just a decade ago, and that's all syphilis. Right, for primary and secondary syphilis, which is the most transmissible type of syphilis, we've seen a 71% increase from a decade ago. And here we are with that. So that's primary and secondary syphilis. And so again, incredibly stark increases you can see from this graph right here of the entire state that we're seeing primary and secondary syphilis rates throughout the entire state. You can see it everywhere. Itasca County, Saint Louis County, Crow County, like all over the southwest and southeast. It occurs throughout the state, right? And then people travel too, so it's not like people are stationary. People travel throughout the whole state. And the reason why we focus again on primary and secondary is that these individuals are most likely to transmit syphilis to others, right? And so here are some numbers. And the point is that we see greater rates in urban centers, but it is throughout the whole state.

Now here are primary and secondary syphilis rates by gender and I want to point out something very striking back in 2015. There were 1.4 cases of primary and secondary syphilis in women per 100,000 people. 1.4. 10 years later, we're almost at 5 cases per 100,000 people, and this is primary in syphilis in females, OK? And there's a point to this and I will get to it. But note that we've seen this stark increase in in, you know, males and females, but it's female when I really want to point out, you can see here this is age specific, primary and secondary syphilis by gender and you can see that it affects all.

Age ranges. You can see there are cases in everyone from 15 all the way to 50 plus this age range of 30 to 39 has the highest rate per population for both males and females. But you can see that there are cases throughout and so it's the most cases we're going to see in that age range of, I would say, 20 to 50 or so, but don't exclude other people like our case earlier with that 68-year-old individual.

And then finally, I want to talk a little bit about primary and secondary syphilis rates by race and ethnicity over time. So, this bar chart demonstrates the breakdown from 2015 to 2024, and the

overall point is historically and currently in 2024, we're seeing disproportionate rates of syphilis cases, primary and secondary in American Indian populations in black, non-Hispanics and Hispanic populations as well. Again, we see this disproportionate impact in these racial and ethnic groups, and it's been since we've started tracking it.

And then finally, I wanna talk a little bit about the number of early syphilis cases and so early syphilis is both primary and secondary. Syphilis, along with those cases that have been diagnosed in the previous year that are currently asymptomatic and as everyone who's been infected within the within the last year. This is by gender and men who have sex with men. This top line here you can see is all men, and so in 2024, 516 males were diagnosed with early syphilis. You can see down here in the lower number in 2024 in the last column, 257 of them identify as MSM. So, if you extrapolate that out, that's about half of all male cases identify as MSM. Right beneath that, you can see 237 females have been diagnosed with early syphilis in 2024 and look at that compared to 2016 on the far-left part of the chart it went from 87 to 237 in a 10-year period. Similarly, if you look at MSM activity, you're looking at 359 cases back in 2016 compared to 257 cases in 2024. These data suggest that what we're seeing is sort of a stabilization or maybe even a slight decrease in cases among individuals who identify as MSM, and an increasing proportion of cases in men who have sex with women and can come and rise in cases in women. This is more hypothesis-generating than anything else, but I do think it's an important thing to look at.

So, we've talked a lot about primary secondary stage. Let's go through staging quickly because staging is important. And so, if you look at this incredibly busy slide, I have put some definitions and how syphilis sort of evolves in an individual over time and so, quickly, primary syphilis occurs about two to six weeks after infection with syphilis, and it's the stage characterized by a chancre, right? So, that's primarily how it's always identified. Secondary syphilis usually happens about two to eight weeks after resolution of the chancre, and it's characterized by a rash and lymphatic and mucous patches and condyloma lata and alopecia. We will get into all of that. And then, those kind of resolve and go away over here, you can see there's about a 15% overlap in symptoms between primary and secondary and sometimes the secondary symptoms are so mild that they're not even noticed or not even recognized by the clinician or even the patient.

Then, we have the diagnosis or the staging of early latent syphilis, which is defined as the infection within the last year and no signs or symptoms, so primary, secondary and early latent all have infection within the previous 12 months. Early latent without symptoms, then we go into latent syphilis, which I should say late latent syphilis, which is infection greater than a year ago where they have no symptoms, and then we have unknown duration of syphilis where we just can't tell when they were infected, but they don't have symptoms, right? Congenital syphilis is infection in utero and then a syphilitic stillbirth, as you can see here, is after 20 weeks gestation or when the fetus weighs greater than 500 grams and the mother had an inadequate treatment or untreated infection.

Now, why are we talking about staging? Why is this important? I'll tell you why. Because treatment is different for early versus late. Early syphilis gets one dose of Bicillin. Late syphilis gets 3 weekly injections. It makes a difference. Syphilis disease is dynamic. It's complex, right?

As noted before, 40% of patients during their symptom infection can have CNS invasion, right? This includes issues with the eyes, the ears, meningeal, vascular, syphilis. 40%: that's severe, right? 25% of patients can have recurrent secondary syphilis, so they can actually be in latent syphilis, late latent, and then revert back with symptoms of secondary syphilis. We think that's what happened in our initial case with that woman, she actually reverted back to secondary syphilis and then down here during the period of latent syphilis. 30% will develop symptoms of tertiary syphilis and we'll get into that as well. The point is that it's a complex and dynamic disease with very, very difficult sort of ways of looking at it and understanding the testing and all that stuff, so we'll get to that.

OK, so clinical presentations. Primary syphilis, as we mentioned before, after infection, this usually develops about two to six weeks after and it heals about four to six weeks after that, right? It's usually a single painless shanker. However, we've seen cases where it's painful. We've seen cases where there's multiple atypical lesions. So, syphilis is always in the differential, but this is what it's going to look like and it's incredibly infectious at this at this stage. So, there's a vulvar lesion right there. Here you can see a very well described chancre on the head of a penis, and it looks like a crater, or I was imagining a swimming pool filled with little spirits swimming around. And then here's a one on the tongue of an individual, so that's how we define primary syphilis. Then, you go into this phase where it's secondary syphilis, and it generally presents two to eight weeks after the primary syphilis and can include, but not always. This is not like you're somebody's going to walk in with all these types of this presentation. Oftentimes it's just generalized lymphadenopathy in a rash, but it can include this Palmer or plant or rash and it kind of looks like this. If you can see that. And then individual the HIV can have an extensive erosive rash as well, so always be concerned. With your patients with HIV as well, you can have condolences which are generally wet and malodorous. Oftentimes they look like warts, but it's that wetness in order that distinguishes them.

Here's a classic example of secondary syphilis with those mucosal patches. You can see sort of that that those areas of clearing you can have that moth eaten patchy alopecia where people will come in.

That's again, these are very classic sort of, you know, textbook images. Most folks don't roll in looking with all these types of symptoms. They can also have sort of like flu-like symptoms. Pharyngitis, adenopathy, myelitis, weight loss. You know, like, general, like, elevated liver enzymes. Think syphilis. It usually subsides after two to six weeks and it can overlap with the primary symptoms of the chancre, right? So, if you see somebody with a chancre and some of these, test them for syphilis, right? These stages also have a high level of infectivity as well.

Let's talk about early latent. So that's infection within the previous 12 months, but they don't have signs of symptoms of primary or secondary syphilis, or they have a positive test less than 12 months after a prior negative syphilis test. So, if they've been tested previously and it's been negative and now it's positive within that within that 12-month period, that's early latent. If they have a fourfold increase in tighter from a previous positive non trip enable test.
And we'll get into all of that. But an increase in the titers of an RPR or a VDRL? If they have report of symptoms consistent with syphilis in the prior 12 months, so if they talk about, you

know, having condyloma lata or something of that nature, or if they've had sexual contact with a known case within the prior 12 months.

Let's talk about late latent syphilis, or latent syphilis under duration. A lot of times you're not going to have any of that information. So, if all of those things were greater than 12 months ago, let's say they had a negative test three years ago and now they have a positive test. I can't say that that positive was in the last year, and if it was greater than 12 months ago or we have insufficient evidence to conclude when the infection was and they don't have clinical signs of primary secondary syphilis, it's gonna be late latent or latent syphilis of unknown duration. And seven here is sort of the same thing, and I'm going to go through it again. It's very similar. It's just over 12 months. But here's the big take home message when faced with uncertainty: you need to think that you don't know it's unknown duration. It may be late, and so we're going to we're going to act conservatively and we're going to treat with three weekly doses of of Bicillin, benzazine, penicillin, and we have to treat it that way.
You have to treat it like it's latent disease.

Let's talk about tertiary syphilis. Very, I would say it's very rare. It's symptomatic late latent syphilis. It can happen 20-30 years after infection. It can result the damage to the heart, blood vessels, liver bones, joints. You get these non-cancerous lesions, and you can see here in this individual he has one sort of over his right cheek and there's another one in the along the palate of that individual's mouth. And it happens in about, they say, untreated syphilis in 30% of cases.

Let's talk about neurosyphilis, otherwise known as complicated syphilis. This is when the syphilis goes into the central nervous system, right? Again, emphasis is up to 40% of cases, OK? Untreated, it can progress to you can have a meningovascular syphilis or a stroke and other neurological complications. It can lead to permanent blindness. It can lead to permanent hearing loss or severe tinnitus. So, every single person you that test positive for syphilis, we have to screen for evidence of neuro syphilis, right? And so ask them about changes in vision or photophobia or discomfort in the eyes or changes in the hearing. Oftentimes there will be this like this acute sort of like onset of tinnitus, headache, stiff necks, anything that could suggest that this individual is having invasion of the CNS. Because if screening is positive, we need to involve our specialists: IDEND, ophthalmology. They need to look and see whether or not it truly is neurosyphilis that's causing these symptoms and then hospitalization and again it's a different treatment for neuroinvasive disease than it is for regular syphilis.

So, let's get to the hard part, testing for syphilis. Let's go over really quick syphilis test treponemal versus non-treponemal. There's two types of serologic tests using only one of them is insufficient, because each test has limitations, and so you need to use a combination of both treponemal tests and non-treponemal tests. So, we'll go through them nonetheless. It's RPR or VDRL usually. Most of the time I think people use RPR. It's quantitative. So what? Report out titers, right? It often correlates with disease activity, and we can use them to follow treatment response. Here's the key. You need a fourfold change in tighter using the same serologic test to demonstrate a clinically significant difference between two different test results, right? And so you're looking for a fourfold change. So, example 1 to 16 to one four or 1:00 to 8:00 to 1 to 32. Something like that. That's really what we're looking for. And then non-treponemal test titers

usually decline after treatment and sometimes become non-reactive with time. However, sometimes non troubling tests remain positive, and it's known as a serofast state, and we'll get into that. And then in combination with the non-treponemal test, there are also treponemal tests, right. And the most common ones I think are probably EIA's and TTPA's. Oh, sorry, TPAS, I spelled that wrong. It's a qualitative result. So, it's either gonna be positive or it's gonna be negative, right? People with a reactive, non-treponemal test. So, like an RPR or BDRL should always receive a treponemal test to confirm the diagnosis of syphilis. OK. So, if you get a positive RPR, you need to get a treponemal test to confirm it, right? People with a reactive treponemal test will have a reactive test for forever. Most people OK. And so, if it was positive, if you were treated with syphilis and you get a treponemal test is gonna be positive, it doesn't necessarily mean that it's a new infection or something like that. And then treponemal tests are generally performed to confirm those non-treponemal reactive results. So, the results from the RPR and then also at the recent onset of a suspicious new lesion, right? And so let's go through the algorithms, OK. Here we go.

This is what's known as the traditional syphilis testing algorithm. You start with a non-treponemal test like an RPR or a VDRL. The quantitative one, right? If that's positive and you can see that -- little green circle with a plus on it. If that's positive, you confirm it with a treponemal test like an EIA or a TPPA or another one, right? And if that's positive, then you can say, OK, we're going over that box. However, if the RPR is negative and I'm going to pop something in here really quick, is that early infection a negative RPR? You have to think, is this too early for the RPR to have converted positive? Is it an early infection? And what you do is you think if clinical signs point to incubating or suspected primary syphilis, right? So if we have a known exposure, or maybe if there's evidence of an incubating primary syphilis: treat. Treat with an IM dose of penicillin G.

What about a serofast state? So, if that RPR is positive, we have to consider serofast state because remember, the treponemal test will always be positive. And so, let's evaluate this clinically. What is the titer of the RPR? Has there been a fourfold change since the previous one? You know, is it sitting at 1:1 or 1:2 and, you know, evaluate clinically, think about is there a hazard going to pass infection and has there been treatment? So, there's considerations when you use the traditional syphilis testing algorithm. Because of that, they came up with this reverse syphilis testing algorithm right where you start with a treponemal test, right? Usually EIA or one like that, and if that's positive then you go to the quantitative non-treponemal test, the RPR or the BDRL, and if that's positive then you do that. However, same thing applies if you have a negative EIA or a CIA. You think: Is this just too early? Have we not yet had an infection to develop the antibodies that would turn this positive? So, if clinical signs point to incubating again, treat with penicillin G, right? And you also have to think about that serofast state. Remember these treponemal tests will usually always remain positive, and so that quantitative RPR comes back, and if it's one to two and we don't see that fourfold change, we have to evaluate clinically and say is this just past infection that we're looking at? Do we need to treat this infection?

So, we'll talk really quickly about serofast state. Generally, after syphilis treatment you expect a non-treponemal titers like RPR BDRL to decrease at least fourfold, usually to non-detectable levels. However, there are individuals that are adequately treated for syphilis that can have a

persistently positive, non-treponemal test, often seen in individuals who are pregnant or who are immunocompromised but can occur in other people. It does not correlate with a new infection, a new infection again has to have that increase in a fourfold increase in titers like 1:4 to 1:16. That would be evidence of an acute infection and then reminder that that treponemal test the EIA or the TPBA will remain positive in most individuals.

Let's talk quickly about false negative results due to the prozone effect. These are PRS, I tell you for non-treponemal tests like an RPR, a prozone effect can occur which would turn the RPR negative. Now, nonetheless require an agglutination of antigen antibody, binding complexes and I put a little diagram here and I'll show you the agglutination happens over here when what we have is we have antibodies binding to different antigens on the surface of the spirochetes and they bind together, and they form these sort of precipitates that come on out and allow you to diagnose using this test. However, if there's so many antibodies, the antibodies bind to all the antigens individually and then there's no cross linking and no agglutination, and so these never precipitate out, and so you'll get an RPR that's negative, right? It's fairly rare, but it does happen. If you have a high suspicion of early infection, you can treat or you can also request serial delusions from your lab to sort of to dilute the number of antibodies out there to formulate this crosslinking and subsequent agglutination.

So, all right, let's get to the good stuff. Let's get to treatment. Treatment's great because in primary, secondary or early latent, it's a single shot of Bicillin, of benzazine penicillin G.
If they report a true allergy, a true verified penicillin allergy, and I and I won't go into it, but I if it's truly an allergy to penicillin, you can use doxycycline twice a day for 14 days. And so the difficulty with that is obviously compliance. It's hard to take medications for two weeks.
Now the difference is late syphilis, so that's late, late and syphilis or syphilis of unknown duration, right. So, if we don't know, we're going to treat them with three weekly injections of of Bicillin. Difficulty with that is, is getting people to come back right and so adequate treatment for late, late into or syphilis of unknown duration can be difficult. But it requires 3 weekly injections of Bicillin. Again, if there's true or verified penicillin allergy, you can use doxycycline, but this is twice a day for 28 days. Remembering to take doxycycline twice a day for 28 days can be challenging, so there's always that. Of note, if the individual is pregnant, only penicillin can be used. That individual has to be desensitized. Work with your allergist.

Now for neuro syphilis, including ocular syphilis and neurosyphilis and this is consultation in conjunction with infectious disease and hospitalized patients. All that kind of stuff. But they need to receive aqueous crystalline penicillin G through IV, either continuous or every four hours, for 10 to 14 days. If they have a penicillin allergy, you really should just desensitize them in consultation with that allergist. Pregnant women have to be desensitized and treated with pen G. And then there are some, not recommended, but there are some case reports of individuals treated with either ceftriaxone or doxycycline for neurosyphilis, but that's again in consultation with infectious disease. And so as a reminder, we're talking about neurosyphilis. 40% of syphilis cases will have neurologic invasion at some point and complicated.

This evidence of in neurosyphilis with ocular or auto manifestations is a medical emergency. We need to get specialist consultation and hospitalization done.

I'm constantly looking at time. It's 12:40 and so I am going to move on. I'm going to talk about mysterious case number two and I'm going to kind of blow through this one pretty quick. But what we have here is we have a 20-year-old black, non-Hispanic female resides in the metro. She has a past medical history of positive gonorrhea that was treated with both IM ceftriaxone and azithromycin. In November, she takes a pregnancy test and is positive. At home, she has her first prenatal visit at 13 weeks and her second prenatal. Visit at 19 weeks. They tested for syphilis and it's reactive with an RPR of 1 to 8. OK. So, she receives her three doses at week 22. She has the 3rd and final dose of her penicillin, right, so that's great. Adequately treated, we consider at 23 weeks just one week later, her titers are at 1:00 to 4:00. It's not a fourfold reduction, it's going down. It's pretty soon to be testing titers after that. After that last sort of dose and so is it trending down or kind of what's going on? So, we'll see. Anyway, she had nine more prenatal visits completed prior to her delivery, so this is great. So at 40 weeks, 3 days she delivers. Spontaneous rupture membrane. She had her vaginal delivery apgars of 8/9. The infant is a little bit large for gestational age. However, during delivery, the provider observed labial lesions that were yellowish white, and they were raised and well demarcated. The infant was subsequently sent to the NICU and due to these vaginal lesions, an IV penicillin for the neonate was started empirically. Good idea? I think it's a good idea. OK, after delivery, the maternal lesions were biopsied and sent for testing. They also tested the infant for all sorts of infectious diseases. They did service swabs and blood and CSF. They tested the CSF for syphilis and was RPR negative also with serum. Complete blood count was not nothing on it, and they did not obtain long bone X-rays, which, if you have concern for congenital syphilis, you would do on infant day two, his herpes workup results returned. The surface, it was negative for both herpes one and two. His serum PCR was negative, however. His cerebral spinal fluid PCR were positive for herpes simplex virus one. Oh, well, now we have it. Penicillin stopped high dose, acyclovir started good idea. I would question that because biopsies on the infant day 10, biopsies and maternal age return confirming syphilis, right? Numerous treponema organisms were in there. They considered this a maternal reinfection, and they're going to treat the infant with 10 days of IV penicillin, which is appropriate. OK. Now remember, the mom had treatment during her pregnancy, right? But Mom was re informed of this potential for reinfection and told her to say you got to come back for treatment and so nine days afterwards, mom came back and got another shot of the by selling. And then she received another test for syphilis nine months later, and she had a titer of 1:1. So basically, she had a reduction, then a fourfold from that previous title that she had. So there's lots in here that we can talk about and there's a reason why I'm presenting this entire case. And so anyway, so the mother of the baby followed up the recommendations and at three months the baby was RPR negative. Although the TPPA was positive and that was due to the maternal antibodies crossing the placenta. During that time, the father of the baby did not receive testing or treatment during the pregnancy. He was notified of his positive syphilis but refused treatment right during the pregnancy, 21 days after delivery. However, the father of the of the baby presented at the clinic for testing and treatment. His titer was 1:256. Stage was unknown. So, he got one dose, but he was lost to follow up and never received the recommended 3 doses.

So let's talk about congenital syphilis and there's all sorts of stuff in that case to unpack. And I we're not gonna have time. But you can imagine, all the different things that happened that contributed to that baby being infected with syphilis. And so congenital syphilis is infection with T pallidum during pregnancy. Early untreated syphilis and mother, right. And so that's within the first year and it's not treated. There's an approximate 80% chance that that baby is going to be infected if you have late, untreated syphilis in mother, right? And so that's after that one year, right after infection, there's about 25% chance of neonatal infection. It is imperative to screen the mother of the baby three times during pregnancy. At the first prenatal visit, usually in the first trimester at 28 to 32 weeks, so that if we do identify syphilis, we can get treatment completed or started before delivery, and then at delivery as well, right? We have to do with those three times due to that risk of reinfection.

The likelihood of infection in the need of treatment are based on several factors, including, obviously, mother syphilis status, the adequacy of internal treatment, all that kind of jazz right now. One difficult thing is that the maternal treponemal and non-treponemal IG antibodies, they both passed the placenta. So that can make babies test interpretation difficult. So, a horrible case. We hate babies infected with syphilis, but how common is this right? So let's go to the EPI. Here we go.

In in the early 2000s, you could see that the number of female early syphilis cases in Minnesota hovered somewhere between I would say two and like 14, right? There's really not that many early syphilis cases, and that's females, all females, primary, secondary or early latent syphilis, right? We're talking just a handful, right, and suddenly right around 2015, things started to skyrocket to a high in 2022, 345 cases. 2024 were down to 237, but there's a couple of reasons I think for that. These are astronomically high numbers compared to where we were. There's two in 2007, 41 in 2014 and you can see it just went up from there. Now, can common rise of congenital syphilis cases also happen during that time period? Here you can see from 2015 to 2024 we were at like two cases in 2015, two cases of congenital syphilis in 2017. We're up to 29 cases in 2024 and we'll probably be at that again in 2025. The rates of cases have skyrocketed as well. This has become an increasingly huge problem nationwide too. I mean, CDC just released a report in 2024 that demonstrated that rates of chlamydia and gonorrhea are actually decreasing, but congenital syphilis continues to remain elevated. It's awful. And so here I put in there were seven congenital syphilis cases prior to 2015. From 2006 to 2015, 27 from 2016 on this chart until 2024, there's 137. So to go from a 10 year period where there's seven to a 10 year period where there's 137 is striking to say the least.

So, OK, clinical manifestations. Infection can result in miscarriage. Still, birth or death shortly after birth in those with untreated early syphilis is estimated to be up to 40% of those pregnancies, you can have a wide spectrum of other clinical manifestations. You know, obviously, preterm birth, low birth weight you can have the evidence of skin desquamation, snuffles, jaundice, thrombocytopenia. A lot of other laboratory abnormalities. You can have development of neurological deafness. You can have cranial abnormalities, bowing of the shins. There's all sorts of stuff, but here's the kicker too. You can also be asymptomatic at birth. Even if you're asymptomatic at birth, you can have, umm, late manifestations, right? And so those are like things like those bony abnormalities in the face, Hutchinson's teeth, ocular abnormalities, hearing loss. We have to screen. We have to screen and find these individuals so

that we can treat them effectively, OK. Here's your obligatory clinical pictures you can see on the left. Here is evidence of desquamation of that of the epidermis and on the right is that classic picture of snuffles that you will see in an infected child. Treatment of congenital syphilis and stuff. So congenital syphilis requires 10 days total of aqueous crystalline penicillin G, right? The baby has to be in the hospital and has to receive IV penicillin for 10 days right again. Desensitization is required for any evidence that there may be a penicillin allergy now based upon.

How likely it is that there is congenital syphilis? There are different guidelines. I'm not going to go into them here, but for full recommendations, I would go to the 2021 CDC STI treatment guidelines and if you want further clarification for any of the stuff. It's all in there.

Remember, congenital syphilis: it requires hospitalization and ID consultation, right? And then it is critical. Here's the big point critical to treat both the mother of the baby and any sexual partner during the pregnancy to prevent reinfection of the mother during pregnancy and subsequent transmission to fetus. I will say that in this case the mother she went to all of her prenatal care visits, she did everything she was supposed to do and it was that risk of reinfection that ended up causing that baby to end up with congenital syphilis.

OK, syphilis screening and prevention. This is the heart of the matter right here. MDH recommends syphilis screening for everybody aged 18 to 49 at least once, right? You should screen them more often if they request it. If they have a known STI exposure or an initiation of a new sexual activity or partner. You should also screen them if they're under the age of 18 or over the age of 49 if they request it, if they're having sexual activity or a new sexual partner, if they have other risk factors. The point is that everyone should be screened and then people should oftentimes be screened more than once, and so, you know, every time you have an initiation of new sex, every time you have, like, the addition of a risk factor, you should be screened for this. You need to screen all pregnant patients three times during pregnancy. First, prenatal visit 28 to 32 weeks and then again at delivery. We can go through all the risk factors, you know, like substance use, incarceration, unstable housing, you know, MSM, commercial sex workers, you know, history of prior syphilis or other STIs, if they're HIV positive, they should obviously be screened more often. And here’s that where that whole bit about having a relationship with your patients and having a way to do a non-judgmental historical and current sexual history is so critical, right? Literally sitting down, and I know this is this is easy for me to say, but when you're, you know when you're sitting with a patient taking the time to establish that relationship and that trust, and I know oftentimes in the ED or urgent care, we don't have that time, but it is so critical to truly understanding somebody's risk factor and need for screening when in doubt – screen, right? Finally, screening testing should be included as part of a comprehensive sexual health visit.

Let's talk about one of my favorite things, Doxy PEP doxycycline post exposure prophylaxis. This is an incredibly effective way to prevent STI's. What it is is the individual taking one 200 milligram dose of doxycycline within 24 hours. But you can wait up to 72 hours, but sooner rather than later, after unprotected sex. So you have unprotected sex, new partner. You're afraid you might end up with an STI. You take 200 milligrams of Doxy PEP and it has been shown to decrease the incidence of syphilis, chlamydia, and gonorrhea among MSM and

transgender women. Evaluation of effectiveness in other populations is currently ongoing. And so I put that in your in your back pocket and we'll get to it, but and I put a little chart here for summary results and you can see here the relative risk reduction. It's up to 84% relative risk reduction in STIs: Doxy PEP versus no Doxy PEP. I mean, this is really good stuff. It's really effective now. This last trial Dpep Kenya ends up. That was a study that looked at cisgender women taking prep and the STI rate with Doxy PEP versus no Doxy PEP. And they only found a relative risk reduction of 12%, however, there was some concern regarding adherence with this population, and ongoing trials are going on right now, suggesting that Doxy PEP is effective in in other populations as well. That being said, the recommendation is to inform men who have sex with men and transgender women who have had greater than or equal to 1 bacterial STI in the past 12 months: you should let them know about Doxy PEP, including the efficacy, the benefits and risks, you know alternate options to prevent, you know, all that kind of jazz. But let them know, and then consider offering Doxy PEP using shared decision making to both them and all non pregnant individuals at increased risk for bacterial STI's, and to those requesting Doxy PEP. in diagnosed previously or have not disclosed the risk status. Basically, talk to your patients about Doxy PEP as an effective way to prevent bacterial STIs.

I put in a blurb here says you can always talk about, you know, this to those at highest risk for bacterial STIs, you know, transactional sex those with multiple previous STI's, but I would suggest talking to everybody about it because it's that effective. OK, as a reminder, all laboratory confirmed cases of syphilis have to be reported to us. Here's our reporting form. You can find it on this website here if you ever have any questions regarding the Syphilis Reporting forum or syphilis in general, you can always call that number at 651-201-5414 and I'm gonna repeat that number later on. But if you have any questions about reporting or syphilis or testing or questions about anything, you can call that number and someone will help you.

So again, I'm gonna review the key takeaways for this presentation. Syphilis rates continue to be elevated, and cases are occurring throughout Minnesota and all demographic populations, but. They're especially impacting women of childbearing age and certain racial and ethnic populations we're seeing a disproportionate impact in American Indian black, non Hispanic and Hispanic populations.

Minnesota recommends screening all individuals, everybody between the ages of 18 and 49 at least once as part of routine care and more with risk factors. And obviously, as we mentioned before, you can screen outside that age if they have new sex partners, sexual initiations, symptoms, if they request it all that kind of stuff. We need to screen all pregnant people three times during pregnancy. First prenatal visit, 28 to 32 weeks, and again at delivery. This is the key: complicated and neurosyphilis can occur at any stage. It's a medical emergency. Remember, up to 40% of syphilis cases will have neurological involvement at some point. It's best to find them early and treat them early before they can have this complicated the course. But if they're not, we're going to see a lot of complicated neurosyphilis, and we do. Scientific data strongly supports the use of Doxy PEP as a preventive strategy to prevent and decrease incidence of syphilis and other STIs. I can't talk enough about Doxy PEP and syphilis can mimic many diseases and testing results can really be difficult to interpret at times. You know, looking at the tires and looking at where they infected previously and looking at changes

and all that kind of stuff, you could always call us and go through that and always think syphilis it can present in any number of ways.

And so here are MDH resources again.

I'm going to point out that there's that number right there in the middle in bold, 651-201-5414. We can provide assistance with staging because we can access previous test results from other systems. We provide partner services. You know we have disease investigation specialists. We can interview people, identify partners we can link partners to care. I think it's underutilized. We need to get more people involved with our DIS folks. We can provide updated guidance recommendations. You can even talk to me if you really want to, you know, give me a ring. That'd be great. And then I just want to say this is not just me this, there are so many people involved in this. And so here's here's some of the folks that have helped me with creating all this, and the EPI and and the response and all that kind of stuff. And so I just want to say thank you and I put this picture in here because sometimes that's me ha. You know to get this, but I think that as we move forward, we'll be able to sort of the reward is so great to sort of like screen everybody, treat everybody, get people in care. The reward is that great. So and with that I will leave it over to Beth and answer any questions you might have. Thanks.

Nick, do you feel like you have time to take any verbal questions?
I think we do have a few minutes left and we will put, yeah, and we'll. Yeah, we'll put the link in the chat for the evaluation as well. But I am seeing we do have a question about do you have a sense how do providers feel about using?

Yeah, yeah, yeah. Go ahead. Yeah, we gotta couple minutes, yeah.

Doxy PEP for non pregnant, cis women. That's one of the ones in the chat. Let me keep looking.

Yeah, you know, it's interesting.
I have heard from multiple sort of folks that work with populations at increased risk for STI acquisition and they are very they're very comfortable with prescribing Doxy PEP. And I think that the more you work with populations, the more you diagnose and screen and treat STI's, the more comfortable you are with utilization of doxycycline. Not sure, just the general gestalt about like you know, family practice and maybe in settings where they don't have a lot of sort of identification of or screening or treatment of STI's, I'm not sure were but what I have seen so far is that is that people are really asking for it and if you offer it to them, they're like, Oh my God, yeah, I would love like from a from a demand standpoint, I think there's a lot of demand and I think that providers that are working with these populations are utilizing it and are and and are haven't seen any issues with it yet.

So, I'm just actually replying and I'll put more info in in the Q&A to Dylan Daniels. Your question actually MDH and the Metro Healthcare Coalition have been working on the Bicillin recall and shortages and I will try to find really quickly the link to MDH guidance which is a little different from CDCs that does expand that recommendation that you know, for patients that might not be able to adhere, we would still recommend that they get the Bicillin. But if you are at all interested in joining those calls, we are meeting weekly, and so if you want to pop your e-mail in the chat I could certainly get you invited to that if you'd like and then I'm going to quickly look for that link to MDH's guidance on Bicillin right now.

Other questions for Nick? I know we're right at the hour. Looking for that link right now.

Yeah. And if not that you know, I really, really appreciate you guys attending and all that and any questions in the Q&A, what we'll do is we'll go ahead and respond to those and then and then push them out to you some way. I'm not sure, Beth how, but we'll make sure that the questions do get answered. And again, I can't emphasize enough. We're here to answer questions. And so, if you want to give us a ring at any time, happy to talk through individual cases. Happy to talk through issues such as the Bicillin shortage and how we plan to deal with that and all that kind of stuff too.

Great. Well, thank you everyone for joining us. The next webinar is in two weeks, two weeks from today, and that is going to be focused on HIV. So, we hope that you join us for that one and then you know, as Nick mentioned, we will be sending out materials here after the call. Thanks so much for joining us. Hope you all have a good rest of your day.

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