Episode 57: Understanding and addressing syphilis trends in the United States

Josh Casey: Hi, I'm Josh Casey. Welcome to *QuidelOrtho Science Bytes*, your trusted source for diagnostic insights and innovations. Today we're talking about syphilis in the United States, a public health issue that has taken a surprising turn. That's because while early-stage syphilis cases are finally declining in the population, congenital syphilis stubbornly continues to rise. To help us unpack what's happening, why it's happening, how diagnostics come into play and what health systems can do about it, we're joined by Andrea Ott-Vasconi, Director of Scientific Affairs and Regulatory at QuidelOrtho. Andrea holds a Bachelor of Science in Biomedical Engineering from Johns Hopkins University and an MBA from New York University. Most recently, she earned a Master of Public Health from Imperial College London. With over 20 years of experience in the medical device industry, Andrea has worked in many different roles, including product development and clinical marketing. In her current role at QuidelOrtho, she manages a team responsible for the development of educational content, scientific publications and evidence generation. Andrea is passionate about increasing awareness of the clinical value of laboratory tests and their impact on improving patient outcomes. Welcome, Andrea. Thank you so much for being here.

Andrea Ott-Vasconi: Thanks for having me on, Josh. I'm looking forward to the discussion.

Josh Casey: Great, well, let's start with the big picture then. What are we seeing in the latest U.S. syphilis data?

Andrea Ott-Vasconi: I'll start with some good news. While we don't have data yet for 2025, the CDC [Centers for Disease Control] provisional data for sexually transmitted infection surveillance showed a 22% decline in primary and secondary stage syphilis cases reported in 2024 compared to 2023. This marks a second consecutive year of decreases in early-stage infections. However, and this is the critical piece, congenital syphilis cases continue to rise nationally with nearly 4,000 cases reported in 2024. Now, congenital syphilis occurs when a mother with syphilis passes the infection to her baby either during pregnancy or at delivery. It can cause severe multi-system complications in babies, including developmental delays, bone and organ abnormalities, and neurological damage. And the worst-case scenario is stillbirth or neonatal death. Congenital syphilis, however, is completely preventable with timely diagnosis and treatment of the mother during pregnancy.

Josh Casey: So if early-stage syphilis is declining, why isn't congenital syphilis declining as well?

Andrea Ott-Vasconi: Great question. There are three major drivers for this divergence. Number one, gaps in prenatal care access. So many pregnant patients enter care late or inconsistently. Number two, missed or late screening. Most states require only one prenatal syphilis test, even though that doesn't match current clinical recommendations. And number three, late pregnancy acquisition of syphilis. The CDC notes that approximately 5% to 10% of congenital syphilis cases occur after a negative test taken earlier in pregnancy, which underscores the importance of multiple screenings during pregnancy. So cases of congenital syphilis aren't rising because treatment doesn't work. Treatment is extremely effective. It's rising because infections are being missed, especially late in pregnancy when a single test early on is not enough.

Josh Casey: Before we talk about improving detection, can you help us understand the types of syphilis tests available today?

Andrea Ott-Vasconi: Sure. Syphilis diagnosis relies on two types of serologic tests, and both are necessary. One type of test is non-treponemal tests. Examples are the commonly used RPR test, or rapid plasma reagent, and an older test that's still used in some settings called VDRL. So these tests detect non-specific antibodies linked to active infection, and they rise with disease activity and fall with treatment. They can, however, be falsely positive in individuals with an autoimmune disease such as lupus, and a false negative result can also occur with an RPR test if an individual has either very early or late-stage syphilis. So non-treponemal tests are good for telling you how active the disease is, monitoring disease progression and whether treatment is working. Now, the second type of test used to diagnose syphilis is treponemal tests. So examples are *Treponema pallidum* particle agglutination assays, or TPPA for short, enzyme immunoassays, or EIAs, and chemiluminescent immunoassays, CIAs, such as the VITROS™ Syphilis Test. Now these tests detect antibodies specific to the *Treponema pallidum* antigens. And once a person has these antibodies, they typically will test positive for life even after successful treatment. So these tests cannot distinguish an active from a past infection and are not used to monitor treatment response. They're good for confirming infection, either past or present.

Josh Casey: That's interesting. So why do we need both?

Andrea Ott-Vasconi: Because together they tell clinicians whether the infection is active or whether it represents a past or treated infection. And together they help reduce the risk of a false-negative or a false-positive result for an active infection. So that's why CDC recommends using both types together.

Josh Casey: Got it. And so, how do labs put these tests into practice?

Andrea Ott-Vasconi: Well, they follow one of two CDC-recommended algorithms. So a traditional algorithm starts with a non-treponemal test such as RPR or VDRL. If a test is positive, it's confirmed with a treponemal test. This approach is common in smaller labs with manual workflows. And then there's the reverse algorithm. This algorithm starts with a treponemal test such as an EIA or chemiluminescent immunoassay. If it's reactive, then you reflex to a non-treponemal test like RPR. And if the results of those two tests are discordant, if they don't agree, then a second treponemal test is used. So this approach is common in high-volume labs and EDs with automated testing environments. And it's especially good at catching very early, our primary stage, or late syphilis, latent or tertiary stage.

Josh Casey: Given all the testing options, where do we see the biggest missed opportunities, especially with pregnant patients?

Andrea Ott-Vasconi: The biggest gap is in the timing and frequency of testing during pregnancy. So most states require a single syphilis test at the first prenatal visit, but far fewer require repeat screening in the third trimester or at delivery. So, congenital syphilis cases are rising because infections are being missed. Only screening women during the first trimester misses infections acquired later in pregnancy, and risk-based approaches to determining who gets tested often fail to identify many affected individuals. For these reasons and because most congenital syphilis cases are preventable with timely repeat testing, the American College of Obstetricians and Gynecologists, also known as ACOG,

recommends universal testing three times in pregnancy, during the first visit, in the third trimester, and at delivery because so many congenital syphilis cases occur after an earlier negative test. Without repeat testing, late pregnancy infections get missed.

Josh Casey: Okay, so what are some strategies that have worked to increase testing for syphilis?

Andrea Ott-Vasconi: A study was published in 2024 with very compelling evidence for implementing routine opt-out syphilis screening in the emergency department. The study was conducted at a large urban emergency department in Chicago. It was a pre-/post-intervention study comparing two years before versus two years after implementation of the opt-out strategy. And they saw a sevenfold increase in syphilis screening among patients under the age of 65. They saw a 288% increase in presumed active syphilis infections, with most of those patients being asymptomatic for an STI. Amongst pregnant patients, screening increased from 5.9% to 49.9%. And more importantly, pregnant patient diagnoses rose 750%, and none of the pregnant patients diagnosed had presented with symptoms of a sexually transmitted infection. So these findings tell us two things: One, symptom-based testing misses the vast majority of infections, and two, EDs are critical screening points, especially for pregnant patients who may not be in prenatal care.

Josh Casey: Those are really incredible results. So, turning now to health systems, what are the most effective steps they can take right now to help reduce congenital syphilis and protect the population?

Andrea Ott-Vasconi: Three steps stand out. One is to adopt the ACOG recommendations for universal testing three times in pregnancy: first visit, third trimester and delivery, even if state laws don't require it. Two, add EHR prompts for repeat screening during pregnancy. And third, treat every pregnancy-related encounter as a screening opportunity. This could be an ED visit, a jail intake, substance abuse programs or at urgent care. So these steps ensure we don't miss infections that occur later in pregnancy.

Josh Casey: We saw how opt-out HIV screening was one of public health's major successes. How does syphilis compare with that story?

Andrea Ott-Vasconi: Opt-out testing dramatically increased HIV detection and normalized routine screening in healthcare settings. Syphilis fits perfectly into that model. It's often asymptomatic. It spreads silently. Its treatment is simple with the administration of same-day benzathine penicillin. Early detection prevents severe outcomes like congenital infection. So that's why syphilis opt-out testing is the next frontier in population-level infectious disease prevention.

Josh Casey: Thank you, Andrea, for leading this insightful conversation and for breaking down both the problem and the solutions. We hope everyone tuning in found the information useful and informative. The key message here is clear. We have the tools, we have strong evidence, and with consistent and proactive screening, especially repeat screening during pregnancy, we can manage and reverse syphilis trends. Thanks to our listeners for joining today.

If you haven't already, please subscribe to *QuidelOrtho Science Bytes*, our monthly podcast where we spotlight the people and ideas that are advancing the power of diagnostics for a healthier future for all. Until next time, take care, everyone