

Transcript - Episode 41: Syphilis

Andrea: Hello, I'm Andrea Ott-Vasconi and welcome to QuidelOrtho Science Bytes. In this episode, we will talk about an important public health issue, an infection called syphilis that can cause serious health problems if left untreated and that has been on the rise for years in the United States. Here with me today to talk about syphilis and the role of the lab is Doctor Lily Li, Senior Director, Medical Scientific and Clinical Affairs at QuidelOrtho.

Doctor Li leads the teams who are responsible for developing clinical trial strategies, providing medical product oversight and risk evaluation, and producing scientific educational content. She also serves as the company's medical director. Doctor Li has a medical degree from Peking University in China and earned her PhD in immunology from the University of Alberta in Canada. She has provided guidance and applied her expertise to development of several infectious disease in vitro diagnostic tests here at QuidelOrtho.

Thank you, Doctor Li for joining me today.

Lily: Thank you Andrea and it's great to be here.

Andrea: Let's start by discussing the prevalence of syphilis in the United States and why it is currently considered an epidemic.

Lily: Yeah, as you know syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum*. It is an age-old disease that was first recorded in the 15th century in Europe.

The pathogen causing the disease *Treponema pallidum* was discovered in 1905. In the 1990s and before the year of 2000, syphilis was almost eliminated in the United States, but unfortunately, since 2011, the rate of syphilis has increased every year. The recent CDC data show that the rate of syphilis increased by 76% almost 80% from 2018 to 2022. And a one year increase was almost 17% from 2021 to 2022. In the year 2022, more than 200,000 cases of syphilis were reported and this increasing trend is observed in all regions in the United States. So we are currently experiencing a nationwide syphilis epidemic in the United States.

Andrea: In addition, there are also high rates of congenital syphilis. Can you explain what congenital syphilis is and what's driving the large increase in the number of cases?

Lily: Congenital syphilis is caused by vertical transmission from an infected untreated mother to her unborn child or the newborn. Because of the high rate of syphilis in women, it also leads to an increase in the rate of congenital syphilis unfortunately. CDC reports show that from 2021 to 2022, the rate of congenital syphilis increased by about 30%. In 2022, a total number of 3,755 cases of congenital syphilis were reported. This was calculated as 100 congenital syphilis cases per 100,000 live births or one in 1,000. Congenital syphilis can cause serious consequences such as miscarriage, stillbirth, low birth weight and lifelong consequences for the newborns such as blindness, brain and nerve problems.

The 2022 congenital syphilis-related deaths increased by about 25% from 2021 and almost 200% from 2018. So it's doubled. Newborns with congenital syphilis-related signs and symptoms increased to 33% from 2021 to 2022 and the 225% from 2018 to 2022. These are very concerning numbers.

Prenatal syphilis screening is important in reducing congenital syphilis. However, based on a recent CDC report, requirement to perform prenatal syphilis screening vary by state. Most of the states do not have requirements corresponding to the CDC recommendations that all pregnant women should be screened at the first prenatal visit. For those high-risk individuals, tests should be done in the third trimester, and at the time of delivery. In addition, the report also showed that compliance with the state requirements was low, giving the increasing rate of congenital syphilis. This is really a serious public health problem.

Andrea: Let's now shift to the detection of the disease. What are the signs and symptoms of syphilis?

Lily: Patients with syphilis can present with a wide range of symptoms and they are not specific to syphilis. Syphilis is a systematic infection that can be classified into four stages: primary, secondary, latent and tertiary. Primary syphilis is early-stage post-infection and the patient often presents with the painless, single or multiple sores at the site of infection.

In the second stage, patients may see diffused skin rashes often on the palm of the hand or the bottom of the feet. This may be accompanied with the swollen lymph nodes, fever, patchy hair loss and other symptoms. Most patients experience no visible signs and symptoms in the latent stage, but if untreated disease can further advance to the tertiary stage. In this stage, serious multi-organ damage can happen, so this could happen to the heart, the eyes and the brain, and that damage can be permanent.

Andrea: How can testing for syphilis combat the current crisis in the U.S.?

Lily: Syphilis is a preventable and curable disease. The earlier patients receive antibiotic treatment the better the outcome and the more efficient at preventing the transmission. The recommended antibiotic drug for the treatment of syphilis including pregnant women with syphilis is benzathine penicillin G. However, in order to achieve a cure, it is critical for high-risk patients and pregnant women to be tested and the patient would confirm the diagnosis to receive early treatment. In response to the syphilis epidemic in the United States the U.S. Department of Health and Human Services established a federal task force to leverage federal resources to reduce the rate of syphilis and congenital syphilis and also to allocate the resources to support the most impacted.

Earlier this year, the CDC updated the laboratory recommendations for syphilis testing. In this document, the CDC provided new recommendations for tests that can support a diagnosis of syphilis. These tests including serological tests and also methodologies for direct identification of the pathogen, *Treponema pallidum*. The recommendation also provided guidance regarding how to choose among multiple available test methods available and how to establish SOP for sample collecting and processing, how to interpret the test results for laboratory reporting and how to consult and treat the patients. So this is a very comprehensive documentation.

Andrea: And we talked about the importance of testing for syphilis. How is syphilis diagnosed and what are the current recommendations from the CDC?

Lily: Right. Today, the diagnosis of syphilis mainly relies on serological tests. These are the type of tests using serum or plasma samples. There are two types of serological tests for syphilis: treponemal tests and non-treponemal tests. Treponemal tests measure antibodies against the lipoidal antigens. These are the lipid components in cell membrane. They can be found in *Treponema pallidum* membranes but can also be found in membranes of damaged host cells. So, an antibody test is not specific to *Treponema pallidum*. The presence of a non-Treponemal antibody may indicate the active syphilis. However, they may also present in other diseases such as autoimmune diseases like lupus. On the other hand, the Treponemal test, like the VITROS syphilis test, detects antibodies specific to *Treponema pallidum* antigens. The presence of Treponemal-specific antibodies may indicate active syphilis but antibodies are also present in patients with latent syphilis or cured previous infection. Based on the natures of these two types of tests, CDC recommends that the two type of serological tests must be used in conjunction for the diagnosis of syphilis and to distinguish between an active, untreated infection and resolved past infection.

Andrea: Is there a specific sequence in which Treponemal and non-Treponemal tests need to be run?

Lily: Treponemal and non-Treponemal tests can be used in either sequence for the diagnosis of syphilis. The so-called traditional algorithm starts with a non-Treponemal test and if positive, the sample should be confirmed by a Treponemal test. The reverse algorithm on the other hand starts with a Treponemal test and if positive the sample should be followed by a non-Treponemal test. When the reverse algorithm is used, any discordant samples should be further tested by a second Treponemal test that is different from the screening Treponemal test as it detects different antigens. The availability of fully automated high-throughput Treponemal tests such as the VITROS syphilis assay facilitate their use as the initial screening test following the reverse algorithm. This is particularly helpful for labs with a large testing volume. The test results from either the traditional or the reverse algorithm together with the patient's history, clinical signs and symptoms are used to diagnose syphilis and to determine the syphilis status of the patient so that the patient can be treated appropriately.

Andrea: Does the CDC recommend a specific algorithm reverse or traditional?

Lily: No. CDC does not recommend a specific algorithm in their recommendations. In their report published earlier this year, they stated that both the traditional and the reverse syphilis screening algorithms are acceptable. The choice of the preferred algorithm really should be based on the lab's situation and the needs such as laboratory resources, laboratory staffing, space, cost considerations, testing volumes and also the patients they serve. The reverse algorithm may be more appropriate for

labs serving a high-risk population such as STD clinics or in larger labs where an automated platform improves workflow efficiency.

Andrea: Thank you. And now for my final question, what role does the lab have in reducing the rate of syphilis infection and ending this epidemic?

Lily: Yeah. As we just said, since syphilis is a preventable and curable disease, the lab plays a critical role in reducing the rate of syphilis through efficient screening and early detection.

One key strategy is the implementation of opt-out screening where all patients are tested unless they decline. This strategy increases the likelihood of early diagnosis, especially in asymptomatic patients.

As I mentioned earlier, to prevent congenital syphilis the CDC recommends that all pregnant women should be screened for syphilis at their first prenatal visit and those who are at a higher risk, they should be screened again early in the third trimester and at the delivery. According to a CDC report in 2022, the vast majority of primary and the secondary syphilis cases were diagnosed outside the STD clinic. This emphasized the critical role for labs in other healthcare settings including the primary care facilities, emergency departments and the community hospitals. Labs equipped with a fully automated systems like the VITROS platform are essential in enabling high-throughput testing while minimizing manual errors.

Early detection is really crucial in mitigating syphilis transmission. By accurately diagnosing syphilis at the early stage of the infection, labs can help ensure that patients receive timely treatment, reducing the risk of spreading the disease to others and eventually help ending the syphilis epidemic in the United States.

Andrea: Thank you, Doctor Li, for this very insightful discussion today. I hope everyone enjoyed this podcast episode. Make sure to review sections within the podcast description with links to learn more. Based on today's podcast I'll leave you with our pop quiz, which type of testing algorithm may be more appropriate for labs serving a high risk population for syphilis?

Thank you for listening today. Please subscribe to QuidelOrtho Science Bytes, our monthly podcast brought to you by QuidelOrtho Corporation where we are transforming the power of diagnostics into a healthier future for all. Take care.

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