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## Public Health Advisory

### Concerning Syphilis Trends and Updated Guidance on Bicillin-LA Shortage

#### July 10, 2023

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#### **Situation Update:**

The number of cases of syphilis have been increasing at an alarming rate over the last several years. In 2021, 869 primary, secondary, and early latent syphilis cases were reported to Riverside County Public Health, more than double the number of cases reported in 2017. Two-thirds of the cases occurred among gay, bisexual, and other men who have sex with men. Although the number of cases is the highest among the MSM community the greatest percent increase is occurring among women.

Increased incidence among women has led to a significant increase in the number of *congenital* syphilis cases. This increase has also been observed throughout California. In 2019, 446 congenital syphilis cases were reported in California, the highest number of cases since 1993. In 2021, Riverside County reported 42 cases of congenital syphilis, which represents a 55.6% increase in cases since 2019.

Riverside County healthcare providers are also reporting possible delayed diagnosis of ocular neurosyphilis cases. Symptoms of ocular neurosyphilis can include axial hypermetropia, optic papilledema/optic papillitis, blurred vision, and changes in peripheral vision. For patients experiencing neurological or ophthalmologic symptoms, particularly when the diagnosis is otherwise unclear, it is important to consider whether syphilis may be the cause.

The increase in the number of infectious and congenital syphilis cases in Riverside County, particularly in the face of an ongoing national shortage of Bicillin® L-A, is a public health concern and requires immediate attention and assistance from medical providers caring for persons with untreated syphilis, and particularly pregnant persons and women/non-binary persons of reproductive age.

#### **Background**

##### Syphilis

Syphilis is a sexually transmitted Infection (STI) that, if left untreated, can spread to the brain and nervous system, resulting in neurosyphilis. Syphilis in pregnancy can result in significant adverse pregnancy outcomes. Many refer to syphilis as “The Great Pretender”, as its symptoms can look like

many other diseases. However, syphilis typically follows a progression of stages that can last for weeks, months, or even years. Syphilis is classified into four stages: primary, secondary, latent, and tertiary. Each stage has distinct signs and symptoms.

#### **Primary Stage:**

During the first (primary) stage of syphilis, a person may notice a single sore (chancre) or multiple sores. The chancre is usually (but not always) firm, round, and painless. It appears at the location where syphilis enters the body. These sores usually occur in, on, or around the penis, vagina, anus, rectum, and lips or in the mouth. The chancre lasts 3 to 6 weeks and heals regardless of whether a person receives treatment. However, the infection will progress to the secondary stage if the person with syphilis does not receive treatment.

#### **Secondary Stage:**

During the secondary stage, a person may develop rough, red, or reddish-brown skin rashes and/or sores in their mouth, penis, vagina, or anus, as well as on the palms of the hands and bottoms of the feet. This stage generally begins with a rash on one or more parts of the body and might appear when a sore is healing during the primary stage or several weeks after the sore is healed. Condyloma lata are large, raised, gray or white lesions. They may develop in warm, moist areas like the mouth, underarm or groin region. The symptoms of secondary syphilis will go away with or without treatment. However, without treatment, the infection will progress to the latent and possibly tertiary stage of disease.

#### **Latent Stage:**

The latent stage of syphilis is when there are no obvious indications or symptoms. Without treatment, a person can have syphilis in their body for years.

#### **Tertiary Stage:**

During the tertiary stage, syphilis can affect a variety of organ systems, including the heart and blood vessels, as well as the eyes, brain and nervous system. In tertiary syphilis, the disease damages internal organs and can result in death.

### Congenital Syphilis

Congenital syphilis (CS) can have serious health consequences for a baby born to a person with syphilis. In California, it is required to screen for syphilis during the first prenatal visit. Whether or not the pregnant person received prenatal care can determine how CS may affect baby's health. Syphilis in pregnant persons can cause miscarriage, premature birth, and/or stillborn birth.

Congenital Syphilis can cause:

- Low birth weight
- Deformed bones
- Severe anemia
- Hepatomegaly and Splenomegaly
- Jaundice
- Brain and nerve disorders
- Meningitis

- Skin rashes
- Death shortly after birth

Diagnosis of CS can be difficult because maternal nontreponemal and treponemal immunoglobulin G (IgG) antibodies can be transferred through the placenta to the fetus, complicating the interpretation of reactive serologic tests for syphilis among neonates (infants aged <30 days). Therefore, treatment decisions frequently must be made on the basis of identification of syphilis in the mother; adequacy of maternal treatment; presence of clinical, laboratory, or radiographic evidence of syphilis in the neonate; and comparison of maternal (at delivery) and neonatal nontreponemal serologic titers (e.g., RPR or VDRL) by using the same test, preferably conducted by the same laboratory.

Healthcare providers should:

- Screen **all pregnant women** for syphilis at the first prenatal visit.
- **Repeat screening tests early in the third trimester** (28-32 weeks gestational age).
- **Repeat screening tests at delivery** for women due to Riverside County being a county with high rates of syphilis.
- **Test** Any woman who delivers a stillborn infant for syphilis.
- **Treat** syphilis in pregnant women as soon as the infection is identified.

### Neurosyphilis

Neurosyphilis is a central nervous system infection of the brain's meninges, the brain itself, or the spinal cord. It can happen to persons at any syphilis stage, especially if the disease is left untreated or if the person is immunocompromised. The five types of neurosyphilis are:

1. **Asymptomatic neurosyphilis:** neurosyphilis is present, yet the individual has no symptoms.
2. **Meningeal syphilis:** can happen within the first few weeks or first few years after contracting syphilis. Can cause headaches, stiff neck, nausea, and vomiting. There may also be loss of vision or hearing.
3. **Meningovascular syphilis:** can develop from a few months to many years after infection. Symptoms are similar to meningeal syphilis; however infected individuals also suffer strokes.
4. **General paresis:** can develop three to thirty years following syphilis. Individuals have general paresis and may have personality or mood changes.
5. **Tabes dorsalis:** can occur anywhere from five to fifty years after initial syphilis infection. Characterized by limb or abdominal discomfort, muscular coordination failure, and bladder problems. Other symptoms include vision loss, loss of reflexes and loss of sense of vibration, poor gait, and impaired balance.

In all patients with syphilis (or highly suspected of having syphilis), inquire about neurologic, ocular, or optic symptoms and complete a neuro exam. Headaches, new-onset weakness, walking difficulties, memory or cognition problems, and personality changes are all symptoms of neurosyphilis. If clinical indications or symptoms of neurologic involvement are evident (e.g., cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, or motor or sensory impairments), a CSF examination should be performed.

Healthcare providers should:

- **Test** for syphilis in patients who have symptoms compatible with neurosyphilis (axial hypermetropia, optic papilledema/optic papillitis, hearing changes, blurred vision, and changes in peripheral vision) without an otherwise known cause.
- **Treat** patients diagnosed with neurosyphilis, following the [CDC 2021 STI Treatment Guidelines for Neurosyphilis](#)

**Screening Recommendations**

\*For the screening guidance below, Riverside County would be considered a community with high syphilis morbidity

<b>Women</b>	<ul style="list-style-type: none"> <li>• Screen asymptomatic women at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity) for syphilis infection<sup>2,7</sup></li> </ul>
<b>Pregnant Women</b>	<ul style="list-style-type: none"> <li>• All pregnant women at the first prenatal visit<sup>8</sup></li> <li>• Retest at 28 weeks gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy [drug misuse, STIs during pregnancy, multiple partners, a new partner, partner with STIs])<sup>2</sup></li> </ul>
<b>Men Who Have Sex With Women</b>	<ul style="list-style-type: none"> <li>• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection<sup>2,7</sup></li> </ul>
<b>Men Who Have Sex With Men</b>	<ul style="list-style-type: none"> <li>• At least annually for sexually active MSM<sup>2</sup></li> <li>• Every 3 to 6 months if at increased risk<sup>2</sup></li> <li>• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection<sup>2,7</sup></li> </ul>
<b>Transgender and Gender Diverse People</b>	<ul style="list-style-type: none"> <li>• Consider screening at least annually based on reported sexual behaviors and exposure<sup>2</sup></li> </ul>
<b>Persons with HIV</b>	<ul style="list-style-type: none"> <li>• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter<sup>2,6</sup></li> <li>• More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology<sup>2</sup></li> </ul>

**Reporting**

Promptly report all cases of syphilis, including congenital syphilis, to RUHS – Public Health (statutory requirement).

**Bicillin® L-A Shortage (Benzathine Penicillin G) Shortage**

The Centers for Disease Control and Prevention (CDC) and the United States Food and Drug Administration (FDA) have declared a shortage of long-acting penicillin G benzathine injectable

suspension products (Bicillin® L-A), with an estimated recovery in 2024. Healthcare providers can monitor the Bicillin® L-A drug shortages on the [FDA Drug Shortages webpage](#). For clinical questions related to the treatment of syphilis during the Bicillin® L-A shortage, please contact the [STD Clinical Consultation Network](#) or [stdcb@cdph.ca.gov](mailto:stdcb@cdph.ca.gov) by email. If you are having trouble accessing BIC -LA or for more information, please visit our website [www.rivcohiv aids.org/](http://www.rivcohiv aids.org/) or contact us at (951) 358-5307.

### **Treatment Recommendations during the Bicillin-LA Shortage**

Continue to follow California Department of Public Health Treatment Guidelines [Health Advisory: Bicillin® L-A \(Benzathine Penicillin G\) Shortage \(ca.gov\)](#). Prioritize BIC-LA for pregnant persons and infants with syphilis.

#### Pregnant Persons

Benzathine penicillin G is **the only** recommended treatment for pregnant people and infants with syphilis. Prompt and timely treatment of syphilis in pregnancy is nearly 100% effective at preventing the [devastating outcomes of congenital syphilis](#), including stillbirth, early infant death, and long-term morbidity such as blindness, deafness, and bone damage.

#### Non-pregnant Adults

- **Doxycycline 100 mg PO BID x 14 days is an acceptable alternative for those with primary, secondary, or early latent syphilis.**
- **Doxycycline 100 mg PO BID x 28 days is an acceptable alternative for those with late latent syphilis or syphilis of unknown duration.**
- Use of other intramuscular formulations of penicillin, including Bicillin® C-R, are **not** acceptable alternatives for the treatment of syphilis.

Given the current Bicillin® L-A drug shortage, CDPH STD Control Branch (STDCB) recommends the following:

- **Prioritize Bicillin® L-A for pregnant people with syphilis infection (or exposure) as well as for infants exposed to syphilis in utero.**
- **Prioritize Bicillin® L-A for patients with contraindications to doxycycline** (e.g., anaphylaxis, hemolytic anemia, Stevens Johnson syndrome).
- **Conserve Bicillin® L-A by using alternative drugs** for the treatment of infectious diseases (e.g., streptococcal pharyngitis) where oral medications or other effective antimicrobials are available.

For clinical questions related to the treatment of syphilis during the Bicillin® L-A shortage, please contact the [STD Clinical Consultation Network](#) or [stdcb@cdph.ca.gov](mailto:stdcb@cdph.ca.gov) by email. If you are having trouble accessing BIC -LA or for more information, please visit our website [www.rivcohiv aids.org/](http://www.rivcohiv aids.org/) or contact us at (951) 358-5307.

Syphilis is a preventable and treatable disease that can have serious complications when left untreated. Together we can make a difference for the residents and visitors of Riverside County. Thank you for your commitment to the health of the community.

- **Supporting Links**
- CDC: [Neurosyphilis, Ocular Syphilis, and Ootosyphilis \(cdc.gov\)](#)
- CDC: [Detailed STD Facts - Syphilis \(cdc.gov\)](#)
- CDC: [STI Screening Recommendations \(cdc.gov\)](#)
- [Global Sexually Transmitted Infections Programme \(who.int\)](#)
- [STD Facts - Syphilis \(cdc.gov\)](#)
- NIH: [Neurosyphilis | National Institute of Neurological Disorders and Stroke \(nih.gov\)](#)
- CDPH CAPTC: Neuro, Ocular and Optic Syphilis Update by Susan Tuddenham MD, MPH Assistant Professor, Division of Infectious Diseases, Johns Hopkins School of Medicine and Kathleen Jacobson MD, Chief of STD Control Branch California Department of Public Health <https://californiapctc.com/training/sti-clinical-update-webinar-neurosyphilis/>
- CDC: [STD Facts - Congenital Syphilis \(cdc.gov\)](#)
- [Expanded Syphilis Screening Recommendations for the Prevention of Congenital Syphilis Guidelines for California Medical Providers 2020](#)
- **CDPH:** [CDPH Doxy-PEP Recommendations for Prevention of STIs \(ca.gov\)](#)
- CDPH: [Health Advisory: Bicillin® L-A \(Benzathine Penicillin G\) Shortage \(ca.gov\)](#)

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