This guide was created to help educate physicians and healthcare providers on the diagnosis, treatment, and prevention of syphilis. Note that images included in this guide depict the symptoms of STDs and are intended for educational use.
Syphilis is a systemic, sexually transmitted disease (STD) caused by the *Treponema pallidum* bacterium.

**Syphilis Transmission**

Two means of syphilis transmission: sexual and vertical

- **Sexual:** Person to person via vaginal, anal, or oral sex through direct contact with syphilis sores or lesions, known as a chancre. Chancre occurs at the primary stage of syphilis and can be found around the external genitals or anus, in the vagina or rectum, or in or around the mouth.

- **Sexual transmission also occurs at the secondary stage,** mainly by direct contact with mucous membrane lesions such as condyloma lata and mucous patches.

- **Vertical:** From infected mother to her unborn baby via the bloodstream.
Providers should routinely test for syphilis in persons who

- are pregnant (at the first prenatal visit, and at the beginning of the third trimester and delivery if risk*);

- are sexually active men who have sex with men (at least annually and more frequently if risk*);

- are living with HIV and are sexually active (annually);

- are otherwise considered to be at increased risk for syphilis*

*Risk is described in the USPSTF’s syphilis screening recommendations and the CDC STD Treatment Guidelines at www.cdc.gov/std/treatment/. Any person with signs or symptoms suggestive of syphilis should be tested for syphilis. Also, anyone with an oral, anal, or vaginal sex partner who has been recently diagnosed with syphilis should be tested for syphilis.
**Primary Stage**

**Signs and Symptoms**

If left untreated, syphilis progresses in stages. The stages are:

**Primary**

- One or more chancres (usually firm, round, small, & painless but can be atypical, subtle lesions) thought to appear at site of exposure (mainly genital area) ~3 weeks after infection (range 10–90 days).

- Chancres can heal on their own in a few days to weeks, even without treatment.

- Patient is highly infectious, and in utero transmission is likely in pregnant women.

www.cdc.gov/std/syphilis/images.htm

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A: Courtesy of Dr. Joseph Engelman at Sf City Clinic
B: Courtesy of National STD Curriculum
C: Courtesy of CDC, Robert E. Sumpter
SECONDARY STAGE

• Mucocutaneous lesions (most commonly rashes) can occur as chancre(s) fade ~6 weeks after infection (range 3 wks–6 mos).

• Rashes may first appear on the palms of hands or the soles of feet, but typically appear on trunk & other areas of the body.
• Lesions such as condyloma lata, a moist, wart-like lesion found in the genital area & mucous patches on the tongue occur in ~25% of patients.

• Other common findings: lymphadenopathy & constitutional symptoms. Less common: patchy alopecia (~10% of patients) & neurologic symptoms (1–2% of patients).

• Symptoms clear within 2–6 wks but may take up to 3 mos, even without treatment.

• Patient is highly infectious, especially if direct contact with a moist lesion. In utero transmission is likely in pregnant women.
LATENT & TERTIARY STAGES

Early latent:

- Patient has reactive nontreponemal and treponemal tests within 1 year of onset of infection, but no symptoms.
- Patient is potentially infectious, as signs of primary & secondary syphilis can reoccur and go unnoticed.

Late Latent or Latent of Unknown Duration:

- Patient has reactive nontreponemal and treponemal tests $\geq$1 year after onset of infection or onset of infection cannot be determined, but no symptoms.
- Patient is not infectious in late latent stage but may be in latent of unknown duration if onset of infection within past year.
Tertiary:

- Manifestations in skin and bones (gummas), & cardiovascular system.
- Patient is not infectious.

* In utero transmission can occur during ANY latent stage of syphilis but is more likely in early latent stage.
• Neurosyphilis is a site of infection and can occur at any stage of syphilis. The nervous system is infected within hours after infection but it can take weeks or years before symptoms present, if at all.

• All patients with syphilis and neurologic, ophthalmologic, or audiologic symptoms warrant a careful neurological exam and a CSF evaluation via a lumbar puncture (LP).
• All patients at high risk for syphilis presenting with neurologic symptoms should be tested for syphilis and HIV.

• Early neurosyphilis usually presents a few weeks or a few years after onset of infection, and can occur at the primary and secondary stage. It typically manifests as meningitis that can affect cranial nerves (especially VI, VII and VIII), and as meningovascular syphilis which may present with stroke-like symptoms.

• Late neurosyphilis typically presents 10–30 years after onset of infection at the late latent stage. Manifestations include general paresis (chronic meningoencephalitis leading to dementia, muscle weakness and paralysis) or tabes dorsalis (demyelination of the posterior columns of the spinal cord).
OCULAR SYPHILIS

• Ocular syphilis can occur at any stage of syphilis.

• Visual complaints consist of vision loss, blurry vision, eye pain, eye redness, etc.

• Patients at high risk for STIs who present with ocular signs or symptoms should be tested for syphilis and HIV.

• Patients with syphilis & ocular symptoms should receive a careful neurological exam, an ophthalmologic assessment, and CSF evaluation via lumbar puncture.

• Treatment should not be delayed while awaiting the results of tests as severe outcomes, including permanent blindness, have been reported.
CONGENITAL SYPHILIS

- All pregnant women should be tested for syphilis at their first prenatal visit, as required by law in most states.

- Additional testing at the beginning of the third trimester (28 weeks) & at delivery is indicated if the woman is at increased risk or lives in a community with high syphilis prevalence rates.

- Pregnant women diagnosed with syphilis should be treated with penicillin immediately. Treatment ≥30 days prior to delivery is likely to prevent most cases of congenital syphilis. (It may not prevent stillbirth or congenital syphilis in a gravely infected fetus as evidenced by fetal syphilis on ultrasound at the time of treatment).

- All women who deliver a stillborn infant (after 20 weeks) should be tested for syphilis at time of delivery.
• Darkfield examinations & other tests (e.g., PCR) to detect *T. pallidum* directly from lesion exudate or tissue are definitive methods for diagnosing early syphilis and congenital syphilis, though not available in most settings.

• Presumptive diagnosis requires use of 2 serologic tests: a nontreponemal test (i.e., VDRL or RPR) & a treponemal test (i.e., FTA-ABS tests, the TP-PA assay, various EIAs, chemiluminescence immunoassays, immunoblots, or rapid treponemal assays). Persons with a reactive nontreponemal test should always receive a treponemal test to confirm the presumptive diagnosis of syphilis.

• Reverse sequence screening algorithm for syphilis testing is also used. Positive treponemal screening tests are confirmed with a standard nontreponemal test with titer. More information at www.cdc.gov/mmwr/preview/mmwrhtml/mm6005a1.htm.
All positive nontreponemal tests must be quantified at time of treatment, as titers are used to monitor treatment success.

- **Note:** In primary syphilis, nontreponemal serologic tests are only ~75% sensitive.

- **Note:** In primary & secondary syphilis, “prozone effect” is possible (false negative RPR occurring when high antibody titers prevent antibody/antigen lattice formation).

- All patients with positive syphilis serologic tests & a presumptive diagnosis of syphilis must be staged to determine the recommended treatment regimen. *Information needed to determine stage:* complete sexual & medical history including history of syphilis testing/treatment; thorough physical exam; epidemiologic information such as risk factors & sexual partner(s) history of syphilis.

- All patients at risk for syphilis warrant a thorough physical exam & sexual history.
Contact the local health department for information about patient’s syphilis testing history & partner notification.

Report presumptive & confirmed cases by stage, including any neurologic or ocular involvement. Report cases of primary, secondary, early latent or congenital syphilis within 1 working day of diagnosis.
TREATMENT

Primary, Secondary, or Early Latent (<1 year)

• Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent (>1 year), Latent Syphilis of Unknown Duration, or Tertiary Syphilis with Normal CSF Examination

• Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Pregnant women

• Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection. (See CDC STD Treatment Guidelines)
Neurosyphilis, Ocular Syphilis

- Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days
- Additional doses of benzathine penicillin are not indicated in patients with HIV infection.
- Additional doses of penicillin in pregnant women with early syphilis may be indicted if evidence of fetal syphilis on ultrasound.

Note: For treatment information on congenital syphilis and syphilis in children, please see CDC STD Treatment Guidelines at www.cdc.gov/std/treatment/.

Penicillin Allergies

- See CDC STD Treatment Guidelines

Penicillin Shortages

- See www.cdc.gov/std/treatment/drugnotices/bicillinshortage.htm
PREVENTION

• Correct and consistent use of latex condoms can reduce the risk of syphilis when the infected area is covered. Since many primary lesions in the vagina & rectum go unnoticed, consistent condom use for vaginal & anal intercourse can reduce the risk of syphilis.

• If sexually active, the surest way to avoid transmission of syphilis is to be in a long-term mutually monogamous relationship with a partner who has been tested and is known to be uninfected.

• Most partners are unaware that they have been exposed to syphilis until notified by a partner, provider, or health department. Partner notification (a type of partner-based intervention) is a service that can be provided by the local health department.

• Sexual partners of infected patients are very likely to be infected. They should receive preventive treatment per CDC STD Treatment Guidelines at the time of visit, without waiting for diagnostic results.
FOR MORE INFORMATION:

- Visit www.cdc.gov/std/syphilis/treatment.htm
- Contact your local health department
- Call 1-800-CDC-INFO
- Health care providers with STD consultation requests can also contact the STD Clinical Consultation Network. This free service is provided by the National Network of STD Clinical Prevention Training Centers & operates 5 days/week. Information is available at www.stdccn.org
- A web-based self-study syphilis module is available for clinicians at www.std.uw.edu/go/pathogen-based/syphilis/core-concept/all