



*Ready-to-Use*

# STD Curriculum for Clinical Educators

## Syphilis Module

**Target Audience** - Faculty in clinical education programs, including those programs that train advanced practice nurses, physician assistants, and physicians

**Contents** - The following resources are provided in this module:

- **Faculty Notes** (Microsoft Word and Adobe Acrobat formats) - Includes notes that correspond to the slide presentation, a case study with discussion points, and test questions with answers
- **Slide Presentation** (Microsoft PowerPoint and Adobe Acrobat formats)
- **Student Handouts**
  - **Case Study** (Microsoft Word format)
  - **Test Questions** (Microsoft Word format)
  - **Slides Handout** (Adobe Acrobat format)
  - **Resources** (Microsoft Word format)

**Suggested Time Allowance** - The approximate time needed to present this module is 60-90 minutes.

These materials were developed by the Training and Health Communication Branch, Division of STD Prevention, CDC. They are based on the curriculum developed by the National Network of STD/HIV Prevention Training Centers (NNPTC) which includes recommendations from the 2002 CDC STD Treatment Guidelines.

Information on the NNPTC can be accessed at:

<http://www.stdhivpreventiontraining.org>

The 2002 CDC STD Treatment Guidelines can be accessed or ordered online at:

<http://www.cdc.gov/std/treatment/default.htm>



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## **Syphilis** *Treponema pallidum*

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### **Learning Objectives**

Upon completion of this content, the learner will be able to:

1. Describe the epidemiology of syphilis in the U.S.
2. Describe the pathogenesis of *T. pallidum*.
3. Discuss the clinical manifestations of syphilis.
4. Identify the common laboratory tests used in the diagnosis of syphilis.
5. List the CDC-recommended treatment regimens for syphilis.
6. Describe appropriate prevention counseling messages for patients with syphilis.
7. Describe public health measures for the prevention of syphilis.

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### **Lessons**

- I. Epidemiology: Disease in the U.S.
- II. Pathogenesis
- III. Clinical manifestations
- IV. Diagnosis
- V. Patient management
- VI. Prevention

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### **I. Epidemiology**

[Slide 5]

#### **A. Definition**

1. Syphilis is a sexually acquired infection caused by *Treponema pallidum*. Syphilis progresses in stages and may become a chronic infection if untreated.
  - a) Disease is characterized by episodes of active disease interrupted by periods of latent infection.
  - b) Incubation period is estimated to be between 10 and 90 days (average 3 weeks).
  - c) Early clinical manifestations (primary and secondary stages) primarily involve the skin and mucosal surfaces. Latent disease has no clinical signs or symptoms. Late manifestations may affect virtually any organ system.
  - d) Neurosyphilis can occur at any stage of syphilis.

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#### **B. Transmission**

1. Major routes of transmission are sexual and vertical (in utero from infected pregnant woman via hematogenous spread to her fetus).

2. An infected individual is most contagious to sex partners during the primary and secondary stages of his/her infection when lesions or rash are present, and much less so in subsequent stages.

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C. Trends in the U.S.

1. The distribution and trends of syphilis are influenced by biological factors, sexual behaviors, biomedical technology, availability of and access to health care, public health efforts, changes in population dynamics, and sociocultural factors.
2. Historically, syphilis was distributed widely throughout the U.S. in the 1940s, but declined rapidly after the introduction of penicillin therapy and broad-based public health programs.
3. During 1986-90, there was a dramatic 85% rise in the incidence of infectious (primary and secondary) syphilis. Some researchers have linked this increase to the use of crack cocaine. Since then, reported cases of syphilis decreased approximately 15% per year to an all-time low in 2000. The rate of P&S syphilis increased in 2001 and 2002; this increase was observed only in men.
4. By the late 1990s, syphilis rates in the U.S. had declined to a point where public health authorities declared syphilis elimination a feasible goal. CDC developed a national plan to eliminate syphilis, which includes rapid case identification and reporting.
5. Syphilis remains an important problem in the South and, increasingly, in urban areas of the country that have large populations of men who have sex with men (MSM). Recent outbreaks of syphilis in subpopulations of MSM have also been characterized by high rates of HIV co-infection and high-risk sexual behavior.

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D. Graph: Syphilis—Reported cases by stage of infection: United States, 1941-2003

1. The rate of primary and secondary (P&S) syphilis reported in the United States decreased during the 1990s and in 2000 was the lowest since reporting began in 1941.

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E. Graph: Primary and secondary syphilis—Rates by state: United States and outlying areas, 2003

1. Syphilis continues to be concentrated in the southern region of the United States.

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F. Graph: Primary and secondary syphilis—Rates by sex: United States, 1981-2003 and the Healthy People 2010 objective

G. Graph: Primary and secondary syphilis — Male-to-female rate ratios: United States, 1981-2003

1. Over the past few years, the rate of P&S syphilis has increased in men and decreased in women, and the male-to-female rate ratio for P&S syphilis has increased, suggesting an increase particularly among MSM.

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H. Primary and secondary syphilis by race and ethnicity, 1981-2003

1. Syphilis disproportionately affects African Americans and Hispanics, although the disparity between rates in these groups and the rate in non-Hispanic whites has been greatly reduced over the past decade

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I. Graph: Congenital Syphilis—Reported cases for infants <1 year of age and rates of primary and secondary syphilis among women: United States, 1970–2003

1. The continuing decrease in the rate of congenital syphilis likely reflects the substantial reduction in the rate of P&S syphilis in women that has occurred in the last decade.
2. The HP2010 objective of 1.0 case per 100,000 live births is many times greater than the rate of congenital syphilis of most industrialized countries, where syphilis and congenital syphilis have nearly been eliminated.

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## II. Pathogenesis

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A. Microbiology

1. Etiologic agent: *Treponema pallidum*, subspecies *pallidum*
2. *T. pallidum* is a corkscrew-shaped, motile microaerophilic bacterium, which cannot be cultured in vitro.
3. *T. pallidum* is a bit longer than the diameter of a white blood cell (6-20 micrometers) and thin (0.1-0.18 micrometers in diameter).
4. *T. pallidum* cannot be viewed by normal light microscopy.

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B. Image: *Treponema pallidum*

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C. Image: *Treponema pallidum* on darkfield microscopy

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- D. Penetration: *T. pallidum* enters the body via skin and mucous membranes through macroscopic and microscopic abrasions during sexual contact. It may also be transmitted transplacentally from mother to fetus during pregnancy.
- E. Dissemination: Before clinical signs or symptoms appear, and within a few hours after inoculation, the spirochete travels via the lymphatic system to regional lymph nodes and then throughout the body via the blood stream. Invasion of the central nervous system can occur during any stage of syphilis.

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### III. Clinical Manifestations

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#### A. Primary syphilis

1. As some organisms lodge at the entry site, proliferate, sensitize lymphocytes and activate macrophages, a primary lesion or "chancre" develops at the site of inoculation.
2. The chancre is a major indicator of primary syphilis. Chancres progress from macule to papule to ulcer. The chancre is typically painless, indurated, and has a clean base. It is highly infectious and heals spontaneously within 1 to 6 weeks. Multiple chancres occur in 25% of cases.
3. Atypical chancres may occur and can mimic herpes or chancroid. Evaluation of patients with genital ulcers should include a serologic test for syphilis and a diagnostic evaluation for genital herpes. In settings where chancroid is present, testing for *Haemophilus ducreyi* should also be performed.
4. Regional lymphadenopathy is classically rubbery, painless, and bilateral.
5. Serologic tests for syphilis may not be positive during early primary syphilis.

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6. Primary syphilis image: Penile chancre

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7. Primary syphilis image: Labial chancre

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8. Primary syphilis image: Perianal chancre

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9. Primary syphilis image: Chancre of the tongue

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#### B. Secondary syphilis

1. In the secondary stage, generalized or localized skin eruptions with mucosal lesions can occur. These eruptions or rashes may be mild or florid (fully developed), depending on the patient's immune response. The lesions may persist for weeks to months.
2. The secondary stage results from multiplication of the bacteria at multiple organ sites after hematogenous spread.
3. Because the organism grows better at lower temperatures, the most common clinical findings are mucocutaneous.
4. Secondary lesions generally first appear 3-6 weeks after the primary chancre appears. Therefore, primary and secondary stages may overlap.
5. Clinical manifestations:
  - a) A rash occurs in 75%-100% of secondary syphilis cases. The rash can be

macular, papular, squamous, pustular (rarely), or a combination. Rashes are usually nonpruritic, and they characteristically involve the palms and soles. Any new onset macular, papular, or squamous rash should be evaluated to rule out secondary syphilis.

- b) Lymphadenopathy occurs in 50%-86% of cases.
  - c) Malaise is the most common constitutional symptom.
  - d) Mucous patches, present in 6%-30% of cases, are flat patches involving oral cavity, pharynx, larynx, and genitals.
  - e) Condylomata lata (10%-20%) are moist, heaped, wart-like papules that occur in warm intertriginous areas (most commonly, gluteal folds, perineum, perianal), and they teem with spirochetes.
  - f) Alopecia (5%) is patchy, occipital or bitemporal, and causes loss of lateral eyebrows.
  - g) Liver and kidney involvement are rare. Splenomegaly is occasionally present.
- C. Serologic tests for syphilis are usually highest in titer during secondary syphilis.
- D. Relapses of secondary symptoms may occur in up to 25% of untreated patients, usually within the first year of infection.
- E. Note: Signs and symptoms of secondary syphilis often are the first observed clinical manifestation of syphilis in those practicing receptive anal and vaginal intercourse because primary lesions may be located in the anus or vagina and may not be recognized by the patient.

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1. Secondary syphilis image: Papulosquamous rash

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2. Secondary syphilis image: Palmar/plantar rash

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3. Secondary syphilis image: Generalized body rash

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4. Secondary syphilis image: Papulo-pustular rash

[Slide 30]

5. Secondary syphilis image: Condylomata lata

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6. Secondary syphilis image: Nickel/dime lesions

[Slide 32]

7. Secondary syphilis image: Alopecia

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- F. Latent syphilis

1. Eventually the host suppresses the infection enough so that no lesions are clinically apparent. Only evidence is positive serologic test for syphilis.
2. Latent syphilis occurs in two categories:
  - a) Early latent: syphilis infection of <1 year duration
  - b) Late latent: syphilis infection of  $\geq 1$  year duration
3. Periods of latency may occur between the primary and secondary stages, between secondary relapses, and after the secondary stage.
4. Relapses of secondary lesions occur in 25% of cases, usually within the first year.

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#### G. Neurosyphilis

1. Neurosyphilis occurs when *T. pallidum* invades the central nervous system.
2. This may occur at any stage of syphilis, and neurosyphilis can be asymptomatic.
3. Early forms of neurosyphilis usually occur a few months to a few years after infection.
  - a) Clinical manifestations include acute syphilitic meningitis, a basilar meningitis that typically involves cranial nerves III, VI, VII and VIII, or meningovascular syphilis, an endarteritis that presents as a stuttering stroke-like syndrome with seizures.
4. Late forms of neurosyphilis usually occur decades after infection, and they are rarely seen.
  - a) Clinical manifestations include general paresis and tabes dorsalis.
  - b) Serologic treponemal tests are usually reactive.
5. Ocular involvement can occur in early or late neurosyphilis.

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6. Neurosyphilis image: Neurosyphilis - spirochetes in neural tissue

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#### H. Tertiary (late) syphilis (other than neurosyphilis)

1. Without treatment, approximately 30% of patients progress to the tertiary stage within 1 to 20 years of infection. Yet, tertiary syphilis is rare because of the widespread availability and use of antibiotics.
2. Clinically, this final stage may manifest as gummas in soft tissue or viscera, central nervous system lesions, and cardiovascular problems. Gummas are granulomatous lesions, which destroy soft tissue, cartilage, and bone and may be an immunological response to treponemal antigens, although most lesions respond to penicillin therapy.
3. Gummatous lesions may occur in skeletal, spinal, and mucosal areas, eyes, and viscera (lung, stomach, liver, genitals, breast, eyes, brain, and heart). The average onset is 10-15 years after infection.
  - a) The destructive lesions can clinically mimic carcinoma.
4. Cardiovascular syphilis:
  - a) Indicated by pathologic lesions of the aortic vasovascularum.

- b) Clinically presents as ascending aortic aneurysm, aortic insufficiency, or coronary ostial stenosis.
- c) Average appearance: about 20-30 years after infection.

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- 5. Tertiary syphilis image: Late syphilis - Serpiginous gummata of forearm

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- 6. Tertiary syphilis image: Late syphilis - Ulcerating gumma

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- 7. Tertiary syphilis image: Cardiovascular syphilis - Narrowing of coronary ostia in aortus

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I. Congenital syphilis

- 1. Congenital syphilis occurs when *T. pallidum* is transmitted from a pregnant woman with syphilis to her fetus. Untreated syphilis during pregnancy may lead to stillbirth, neonatal death, and infant disorders such as deafness, neurologic impairment, and bone deformities.
- 2. Transmission to the fetus in pregnancy can occur during any stage of syphilis, but the risk is much higher during primary and secondary syphilis.
- 3. Fetal infection can occur during any trimester of pregnancy.
- 4. A wide spectrum of severity exists, and only severe cases are clinically apparent at birth.
- 5. Treatment of the mother during the last month of pregnancy or with a drug other than penicillin cannot be considered adequate treatment for the fetus.
- 6. Congenital syphilis is traditionally classified as either early or late disease. Early manifestations occur within the first two years of life, and late manifestations occur after two years of age. Early manifestations are the most common.
  - a) Early lesions in infants (<2 years old) are usually inflammatory, may involve skin (can be bullous or exudative) or mucous membranes. Can result in alopecia, generalized lymphadenopathy, meningitis, osteitis or osteochondritis, and hepatosplenomegaly. May include hematologic abnormalities such as thrombocytopenia and anemia.
  - b) Late lesions (in children >2 years old) tend to be immunologic and destructive. Lesions most commonly appear as interstitial keratitis. Less commonly result in eighth nerve deafness, bone and teeth involvement (saber shins, mulberry molars, Hutchinson incisors).

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- 7. Congenital syphilis image: Mucous patches

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- 8. Congenital syphilis image: Hutchinson's teeth

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9. Congenital syphilis image: Perforation of palate

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#### IV. Diagnosis

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Aspects of a syphilis diagnosis include clinical history, physical examination, and laboratory diagnosis.

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##### A. Clinical history

1. Obtaining a detailed history is critical for determining the duration of infection and assessing the possibility of reinfection. When obtaining the patient's history, the health care professional should assess whether the patient has had:
  - a) A history of syphilis (if yes, obtain results of previous serologic tests for comparison purposes).
  - b) Known contact to an early case of syphilis.
  - c) Typical signs or symptoms of syphilis in the past 12 months.
2. Determine date and results of patient's most recent serologic test for syphilis, even if the patient reports no history of the disease. This is particularly helpful for evaluating a patient with a low titer serologic test, no symptoms or symptom history, and no known contact to an early case of syphilis.
3. The local health department may be able to provide information on whether the patient has been reported as having had syphilis in the past, including reported serologic test results.

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##### B. A thorough exam includes:

1. Physical examination of oral cavity, lymph nodes, skin of torso, palms and soles, and the genitalia and perianal area for signs of infection.
2. Neurologic exam concentrating on cranial nerves, including II (optic), III (oculomotor), VI, VII (facial), and VIII (auditory).

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C. Laboratory: The definitive methods for diagnosing early syphilis are darkfield microscopy and direct fluorescent antibody tests of lesion exudate or tissue. In the absence of these methods, a presumptive diagnosis is possible with the use of two types of serologic tests: nontreponemal and treponemal.

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1. Darkfield microscopy
  - a) What to look for:
    - 1) *T. pallidum* morphology: spiral shape, with 10-14 coils, 6-20

- micrometers long.
- 2) *T. pallidum* motility: corkscrew motion, bends and flexes at sharp angles and does not lose its convolutions.
- b) Advantages:
- 1) Definitive immediate diagnosis (useful in primary and secondary disease).
  - 2) Rapid results.
- c) Disadvantages:
- 1) An experienced microscopist and specialized equipment (often not available outside of a specialized clinic) are required.
  - 2) Confusion with other pathogenic or non-pathogenic spirochetes may occur. Generally not recommended on oral lesions because of specificity problem with non-pathogenic spirochetes in the oral cavity.
  - 3) Must be performed immediately because motility is important to identification. The sensitivity of darkfield microscopy decreases as the lesion heals.
  - 4) Possibility of false negatives increases with use of topical substances (e.g., soap and water, antibiotic ointments, etc.).

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2. Direct fluorescent antibody - *T. pallidum* (DFA-TP):
  - a) Identifies *T. pallidum* on direct lesion smear by immunofluorescence using polyclonal antiserum or monoclonal antibody.
  - b) Advantages
    - 1) Polyclonal reagent is absorbed to remove most cross-reactive antibody.
    - 2) Compares favorably with darkfield microscopy.
  - c) Disadvantages
    - 1) Turnaround time 1-2 days

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3. Serologic tests for syphilis
  - a) Two types: Treponemal (qualitative) and nontreponemal (qualitative and quantitative)
  - b) The use of only one type of serologic test is insufficient for diagnosis because false-positive nontreponemal test results may occur secondary to various medical conditions (see Slide 64).

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- c) Nontreponemal tests include: VDRL (Venereal Disease Research Laboratory), RPR (Rapid Plasma Reagin), TRUST (Toluidine Red Unheated Serum Test), USR (Unheated Serum Reagin)
  - 1) Principles
    - i) Measure IgM and IgG antibody directed against a cardiolipin-lecithin-cholesterol antigen
    - ii) Not specific for *T. pallidum*
    - iii) Reaction may be microscopic (VDRL and USR) or macroscopic

(RPR and TRUST)

- iv) Nontreponemal test titers usually correlate with disease activity, and the results are reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16 to 1:4 or from 1:8 to 1:32) is considered necessary to demonstrate a clinically significant difference.
- v) The VDRL and RPR are equally valid assays, but quantitative results from the two tests cannot be compared directly because RPR titers are often slightly higher than VDRL titers. TRUST is similar to the RPR, and USR is similar to the VDRL.
- vi) Sequential serologic tests in individual patients should be performed by using the same testing method (e.g., VDRL or RPR), preferably by the same laboratory.
- vii) Nontreponemal tests usually become nonreactive with time after treatment. In some patients, however, nontreponemal antibodies can persist at a low titer for a long period of time, sometimes for the life of the patient. This response is referred to as the "serofast reaction."

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2) Advantages

- i) Rapid and inexpensive
- ii) Can use plasma rather than serum (RPR, TRUST)
- iii) Easy to perform and can be done in clinic or office
- iv) Quantitative
- v) Can be used to follow response to therapy and evaluate possible reinfection

3) Disadvantages

- i) May be insensitive in certain stages (particularly early primary, late latent, and tertiary (late))
- ii) False-positive reactions can occur
- iii) Rarely, a phenomenon called the "prozone effect" may cause a false-negative reaction. The prozone effect occurs when the reaction is overwhelmed by antibody excess. It is most likely to occur in secondary syphilis. If clinical suspicion of secondary syphilis is high, the lab should titer the sample or dilute the serum to a 1/16 dilution and repeat the qualitative test to rule out the prozone effect.

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- d) Treponemal tests include: TP-PA (*T. pallidum* Particle Agglutination), FTA-ABS (Fluorescent Treponemal Antibody-Absorbtion), and EIA (Enzyme Immuno-Assay).

1) Principles

- i) Measures antibody directed against *T. pallidum* antigens by particle agglutination (TP-PA), immunofluorescence (FTA-ABS), or enzyme

- reaction (EIA).
- ii) Qualitative.
- iii) Usually reactive for life, even after adequate treatment. However, 15%-25% of patients treated during the primary stage revert to being serologically nonreactive after 2-3 years.
- iv) Treponemal antibody titers correlate poorly with disease activity, and they should not be used to assess treatment response.

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- 4. Sensitivity of serologic tests in untreated syphilis
  - a) This chart compares the sensitivity of various serological tests by stage of syphilis.

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- 5. Causes of false-positive reactions in serologic tests for syphilis
  - a) False-positive reactions can occur with both nontreponemal and treponemal serologic tests for syphilis.
  - b) This chart lists causes of false-positive reactions for various serologic tests. In addition to those listed on the slide, technical errors and transient unknown causes can lead to false-positive reactions in treponemal and nontreponemal tests.

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- D. Diagnosis of latent syphilis
  - 1. It is sometimes difficult to determine the duration of infection in a patient with latent syphilis. Patients can be diagnosed as having early latent syphilis if, within the year preceding the evaluation, they had at least one of the following:
    - a) A documented seroconversion,
    - b) Unequivocal symptoms of primary or secondary syphilis,
    - c) A sex partner documented to have primary, secondary, or early latent syphilis, or
    - d) The only possible exposure occurred within the preceding 12 months.
  - 2. Patients who have latent syphilis of unknown duration should be managed clinically as if they have late latent syphilis.
  - 3. Public health laws require that all cases of syphilis, regardless of stage, be reported to the state/local health department.

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- E. Central nervous system (CNS) disease diagnostic issues
  - 1. CNS disease can occur during any stage of syphilis.
  - 2. Cerebrospinal fluid (CSF) abnormalities have been noted in 13% of patients with untreated primary syphilis and 25%-40% of patients with untreated secondary syphilis.
  - 3. Conventional therapy is effective for the vast majority of immuno-competent patients with asymptomatic CNS involvement in primary and secondary

syphilis.

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4. Patients who have syphilis and who demonstrate any of the following criteria should have a prompt CSF evaluation:
  - a) Neurologic or ophthalmic signs or symptoms,
  - b) Evidence of active tertiary syphilis (e.g. aortitis, gumma, and iritis),
  - c) Treatment failure, or
  - d) HIV infection with late latent syphilis or syphilis of unknown duration.
5. Some specialists recommend performing a CSF evaluation on all patients who have latent syphilis and a nontreponemal serologic test titer of  $\geq 1:32$ .

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6. No test can be used alone to diagnose neurosyphilis.
  - a) VDRL-CSF is highly specific but insensitive.
  - b) Diagnosis of neurosyphilis usually depends on various combinations of the following factors:
    - 1) Reactive serologic test results,
    - 2) Abnormalities of CSF cell count or protein, or
    - 3) A reactive VDRL-CSF with or without clinical manifestations.
  - c) CSF leukocyte count usually is elevated ( $>5$  WBCs/mm<sup>3</sup>) in patients with neurosyphilis; this count also is a sensitive measure of the effectiveness of therapy.
  - d) The VDRL-CSF is the standard serologic test for CSF, and when reactive in the absence of contamination of the CSF with blood, it is considered diagnostic of neurosyphilis. However, the VDRL-CSF may be nonreactive when neurosyphilis is present (50% sensitivity).
  - e) Some specialists recommend performing an FTA-ABS test on CSF. The CSF FTA-ABS is less specific for neurosyphilis than the VDRL-CSF, but the test is highly sensitive. Therefore, some specialists believe that a negative CSF FTA-ABS test excludes neurosyphilis.
7. For more detailed information on the diagnosis of neurosyphilis including interpretation of CSF findings, consult the 2002 CDC STD Treatment Guidelines or your state/local health department STD Program.

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#### F. Syphilis and HIV

1. Syphilis and HIV infections commonly co-exist.
2. In general, the clinical course of syphilis in HIV-infected patients is similar to that in non-HIV-infected patients.
3. Serologic tests for syphilis are equivalent in sensitivity in HIV-infected and non-infected persons in the vast majority of patients.
4. If clinical suspicion of syphilis is high and the serologic tests are negative, then use of other tests (e.g., biopsy of the lesion or rash) should be considered.
5. Conventional therapy is usually effective.

6. Some investigators think that patients with HIV may be more likely to present with symptomatic neurosyphilis.

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## V. Patient Management

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A. Therapy – The following are 2002 CDC-recommended treatment regimens for syphilis. Refer to the 2002 CDC STD Treatment Guidelines for additional and more detailed information.

1. Primary, secondary, and early latent syphilis in adults without neurologic involvement
  - a) Benzathine penicillin G, 2.4 million units IM in a single dose
  - b) Penicillin allergic: Doxycycline 100 mg orally twice daily for 14 days, OR tetracycline 500 mg orally 4 times daily for 14 days

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2. Late latent or latent syphilis of unknown duration in adults without neurologic involvement
  - a) Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
  - b) Penicillin allergic: Doxycycline 100 mg orally twice daily for 28 days, OR tetracycline 500 mg orally 4 times daily for 28 days

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3. Tertiary (late) syphilis without neurologic involvement
  - a) Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
  - b) Penicillin allergic: Treat according to treatment regimens recommended for late latent syphilis.

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4. Neurosyphilis
  - a) 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 IV
  - b) Alternative regimen (if compliance can be ensured): Procaine penicillin 2.4 million units IM once daily plus Probenecid 500 mg orally 4 times a day, both for 10-14 days.
  - c) Penicillin allergic: Ceftriaxone can be used as an alternative treatment, although the possibility of cross-reactivity between this agent and penicillin exists. Some specialists recommend ceftriaxone 2 g daily either IM or IV for 10-14 days. If concern exists regarding the safety of ceftriaxone for a patient with neurosyphilis, the patient should obtain skin testing to confirm penicillin allergy, if necessary, and be hospitalized, desensitized, and treated with penicillin.

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5. Syphilis in pregnancy
  - a) Treat with penicillin according to stage of infection.
  - b) Erythromycin is no longer an acceptable alternative drug in penicillin-allergic patients.
  - c) Penicillin allergic: Pregnant patients who are skin-test-reactive should be desensitized in the hospital and treated with penicillin.
  - d) Some experts recommend that a second dose of Benzathine penicillin G 2.4 million units IM be administered 1 week after the initial dose for pregnant women who have primary, secondary, or early latent infection.
  - e) Treatment of the mother during the last month of pregnancy or with a drug other than penicillin cannot be considered adequate treatment for the fetus.
  
6. Syphilis in infants and children
  - a) Refer to the 2002 CDC STD Treatment Guidelines or the state/local health department STD program for information on the management of congenital and acquired syphilis in infants and children.

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7. Jarisch-Herxheimer reaction
  - a) Self-limited reaction to anti-treponemal therapy characterized by fever, malaise, nausea, and vomiting. It may be associated with chills and exacerbation of secondary rash.
  - b) Occurs within 24 hours after therapy and usually resolves within 24 hours.
  - c) Patients should be warned that it is not an allergic reaction to penicillin and that it can be treated with symptomatic support.
  - d) More frequent after treatment with penicillin and treatment of early syphilis, especially at the secondary stage.
  - e) Pregnant women should be informed of this possible reaction, that it may precipitate early labor, and that they should notify an obstetrician if problems develop.

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B. Syphilis and HIV/other STDs

1. Some specialists recommend that HIV-infected persons with primary or secondary syphilis receive additional treatments (e.g., Benzathine penicillin G administered at 1-week intervals for 3 weeks, as recommended for late syphilis).
2. Penicillin-allergic patients with syphilis whose compliance with therapy or follow-up cannot be ensured should be desensitized and treated with penicillin. The use of alternatives to penicillin has not been well studied in HIV-infected patients.
3. All patients who have syphilis should be tested for HIV infection.

4. Persons with primary or secondary syphilis who live in areas with a high prevalence of HIV should be retested for HIV after 3 months if the first HIV test result was negative.
5. Consider screening persons with syphilis for other STDs based on risk.

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C. Follow-up

1. Patients treated for primary or secondary syphilis should be re-examined clinically and serologically 6 months and 12 months following treatment. Earlier clinical follow-up should be considered in certain circumstances (e.g., pregnancy) to ensure improvement and resolution of symptoms.
2. Follow-up titers should be compared to the maximum or baseline nontreponemal titer obtained on day of treatment.
3. Patients with latent syphilis should be followed up clinically and serologically at 6, 12, and 24 months.
4. HIV-infected patients should be evaluated more frequently (i.e., at 3, 6, 9, 12, and 24 months for HIV-infected patients with primary or secondary syphilis; at 6, 12, 18, and 24 months for HIV-infected persons with latent syphilis).
5. Neurosyphilis: serologic testing as above, with repeat CSF examination if CSF pleocytosis present initially, at 6-month intervals until normal.
6. Recommend HIV test for all patients with syphilis and consider retesting in 3-6 months if initially negative.

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7. Treatment failure

- a) Indications of probable treatment failure or reinfection include:
  - 1) Persistent or recurring signs or symptoms.
  - 2) Sustained fourfold increase in nontreponemal titer.
  - 3) Failure of nontreponemal titers to decline fourfold within 6 months after therapy for primary or secondary syphilis.
- b) These patients should be re-treated and re-evaluated for HIV infection. Because treatment failure may be the result of unrecognized CNS infection, some specialists recommend CSF examination in such situations.
- c) When patients are retreated, most STD specialists recommend weekly injections of Benzathine penicillin G 2.4 million units IM for 3 weeks, unless CSF examination indicates neurosyphilis.
- d) Refer to the 2002 CDC STD Treatment Guidelines for more detailed information on assessment and management of probable treatment failure.

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**VI. Prevention**

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A. Patient counseling and education

1. Patient counseling and education should include the following topics:
  - a) Nature of the disease
    - 1) Syphilis may be symptomatic or asymptomatic.
    - 2) Because syphilis is a systemic infection, extra-genital symptoms (such as rashes and alopecia) may occur.
    - 3) Untreated syphilis in pregnancy can lead to death or severe disability in the fetus.
    - 4) Sequelae of untreated syphilis include neurologic and cardiovascular disorders.
  - b) Transmission
    - 1) Syphilis is transmitted sexually or vertically (from pregnant mother to fetus).
    - 2) Syphilis is most infectious during the primary and secondary stages (when lesions or rashes are present). However, lesions may be inapparent.
    - 3) All at-risk sex partners need to be evaluated and possibly treated.
    - 4) Syphilis is associated with increased susceptibility to HIV acquisition.
  - c) Treatment and follow up
    - 1) If treated with penicillin, the Jarisch-Herxheimer reaction may occur.
    - 2) Return for follow-up serology at 6 and 12 months (every 3 months if HIV positive).
    - 3) The patient may be “serofast” or have positive treponemal and nontreponemal serologic tests for life.
  - d) Risk reduction
    - 1) Assess the patient’s potential for behavior change.
    - 2) Discuss prevention strategies such as abstinence, mutual monogamy with an uninfected partner, use of condoms, and limiting the number of sex partners.
    - 3) Discuss latex condoms, which when used consistently and correctly, can reduce the risk of syphilis transmission only when the infected area or site of potential exposure is protected. Genital ulcer diseases, including syphilis, can occur in male or female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered.
  - e) Develop individualized risk-reduction plans.
2. Public Health Measures for the Prevention of Syphilis

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- a) Management of sex partners
  - 1) Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, these lesions may be clinically inapparent. Persons sexually exposed to a patient with syphilis in any stage should be evaluated clinically and serologically.

- 2) At-risk sex partners are determined based on the patient's diagnosed stage of disease. Partners exposed during the following time periods before the patient receives treatment should be considered at-risk:
  1. Primary: 3 months plus duration of symptoms  
Secondary: 6 months plus duration of symptoms  
Early latent: 1 year
- 3) Presumptive treatment should be given to those persons who were exposed within the 90 days preceding a sex partner's diagnosis of primary, secondary, or early latent syphilis, because they might be infected, even if seronegative.
- 4) Persons who were exposed >90 days before a sex partner's diagnosis of primary, secondary, or early latent syphilis should also be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- 5) For purposes of partner notification and presumptive treatment of exposed sex partners, patients with syphilis of unknown duration who have high nontreponemal serologic test titers (i.e.,  $\geq 1:32$ ) may be considered as having early syphilis. However, serologic titers should not be used to differentiate early from late latent syphilis for the purpose of determining treatment.
- 6) Long-term sex partners of patients who have latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the findings of the evaluation.

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b) Screening

- 1) Pregnant women should be screened and counseled at least at the first prenatal visit.
  - i) For communities and populations in which the prevalence of syphilis is high, or for patients at risk, serologic testing should be performed twice during the third trimester, at 28 weeks, and at delivery, in addition to routine early screening.
  - ii) Any woman who gives birth to a stillborn infant after 20 weeks gestation should be tested for syphilis.
  - iii) No infant should leave the hospital without the maternal serologic status having been determined at least once during pregnancy and preferably again at delivery.
- 2) Other populations should be selected for screening based on local prevalence of syphilis and the patient's risk behaviors. Contact your state/local health department for populations at risk and for screening recommendations in your area.

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c) Reporting

- 1) Laws and regulations in all states require that persons diagnosed with syphilis be reported to public health authorities by clinicians, labs, or

both. The follow up of patients with early syphilis is a public health priority.

- 2) Patients with primary, secondary or early latent syphilis, or syphilis of unknown duration with a high nontreponemal serologic test titer (i.e.,  $\geq 1:32$ ), should be referred to the local health department STD program for interview, partner elicitation, and partner follow up.

## CASE STUDY

[Slide 78]

Stan Carter is a 19-year-old male who presents to the STD clinic because he's had a sore on his penis for 1 week.

### History

- Came to the STD clinic with a chief complaint of a penile lesion that had been present for 1 week.
- Last sexual exposure was 3 weeks prior, without a condom.
- No history of recent travel.
- Predominantly female partners (3 in the last 6 months), and occasional male partners (2 in the past year).
- Last HIV antibody test (2 months prior) was negative.
- Has 3 children with 2 different women.

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### Physical Exam

- No oral, perianal, or extra-genital lesions.
- Genital exam shows an uncircumcised penis with a lesion on the ventral side near the frenulum. Lesion is red, indurated, clean-based, and non-tender.
- Two enlarged tender right inguinal nodes, 1.5 cm x 1 cm.
- Scrotal contents are without masses or tenderness.
- No urethral discharge.
- No rashes on torso, palms, or soles. No alopecia. Neurologic exam WNL.

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### 1. Based on Stan's history and physical exam, what are the possible etiologic agents that should be considered in the differential diagnosis?

Correct responses include the following, which are characterized by genital ulcers:

- Herpes Simplex Virus (HSV) – HSV is the most common cause of genital ulceration in the United States and should be considered.
- *Treponema pallidum* – With Stan's history, well-circumscribed indurated ulcer with a clean base, and regional lymphadenopathy, syphilis, caused by *T. pallidum*, should be part of the differential diagnosis.
- *Haemophilus ducreyi* – Although rarely seen in the United States, chancroid, caused by *H. ducreyi* and characterized by painful lesions with irregular borders, could be part of the differential diagnosis.
- Lymphogranuloma venereum (LGV) – Although rarely seen in the U.S., LGV, which causes a relatively innocuous painless and superficial ulcer, could be part of the differential diagnosis.

### 2. What is the most likely diagnosis?

Primary syphilis. With this history and well-circumscribed, indurated ulcer with a clean base, primary syphilis is the most likely diagnosis. Primary syphilis most often produces

an indurated (raised with slightly firm edges) genital lesion with a clean, friable base. Although generally painless, lesions can become painful and purulent if superinfected. Tender or non-tender unilateral or bilateral lymphadenopathy may be present.

Other diagnoses are less likely:

- HSV – While it's the most common cause of genital ulceration in the U.S., herpes lesions are initially vesicular, with an erythematous border. Herpes lesions typically are painful but may be pruritic and have only minimal associated tenderness if recurrent. As lesions progress, they can become purulent or appear as shallow ulcerations. They are often grouped but can occur as a single lesion. Tender inguinal adenopathy may be present.
- Chancroid – Chancroid lesions are uniformly painful and often have an irregular border. They are deep, with a purulent, necrotic, “dirty” base, and are not indurated. There is usually associated lymphadenopathy that can coalesce and form a fluctuant tender bubo. Chancroid is not frequently encountered in the U.S., but it is still seen in certain urban areas.
- LGV – LGV causes a relatively innocuous, painless, and superficial ulcer which often goes unnoticed. Patients generally present because of enlarged and tender inguinal nodes. LGV is not frequently encountered in the U.S.

### **3. Which laboratory tests would be appropriate to order or perform?**

Tests to confirm the diagnosis of syphilis or to rule out other possible pathogens would be appropriate. These tests include the following:

- A stat RPR, if the capability exists.
- Darkfield microscopy, if the capability exists. It can identify *T. pallidum* directly on serous material taken from the lesion.
- Treponemal serologic test for syphilis (e.g., FTA-ABS) – should be accompanied by a nontreponemal test because the use of only one type of serologic test is insufficient for diagnosis.
- Nontreponemal serologic test for syphilis (e.g., RPR) – should be accompanied by a treponemal test because the use of only one type of serologic test is insufficient for diagnosis.
- HSV tests – Cultures, DNA probes, or antigen detection tests for HSV as available would be appropriate.
- HIV counseling and testing should be considered, even if his test from 2 months ago is negative, because the patient is high risk, and the result may impact follow up. HIV counseling and testing is appropriate for any patient with an STD, especially those STDs characterized by lesions.
- Tests for other STDs, such as gonorrhea and chlamydia – Patients suspected of having an STD should be screened for other STDs.

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The results of stat laboratory tests showed the following:

RPR: Nonreactive

Darkfield examination of penile lesion: Positive for *T. pallidum*

#### **4. What is the diagnosis?**

The diagnosis is primary syphilis. The identification of *T. pallidum* on darkfield examination confirms the diagnosis.

A positive RPR is not required for the diagnosis. Serologic tests for syphilis, such as RPR, may be nonreactive, particularly in early primary syphilis.

#### **5. What is the appropriate treatment?**

The appropriate treatment for primary syphilis in an adult is Benzathine penicillin G 2.4 million units IM in a single dose.

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The results from the reference laboratory showed the following:

RPR: Nonreactive

FTA-ABS: Reactive

HSV culture: Negative

Gonorrhea culture: Negative

Chlamydia DNA-probe: Negative

HIV antibody test: Negative

#### **6. Do the reference laboratory results change the diagnosis?**

No. The identification of *T. pallidum* on darkfield examination confirms the diagnosis of primary syphilis.

A positive RPR is not required for the diagnosis. Serologic tests for syphilis, such as RPR, may be nonreactive, particularly in early primary syphilis.

#### **7. Who is responsible for reporting this case to the local health department?**

Laws and regulations in all states require that persons diagnosed with syphilis be reported to public health authorities by clinicians, laboratories, or both. The follow up of patients with early syphilis is a public health priority. Check with your local health department for reporting requirements in your area.

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#### **Partner Management**

Stan had the following sex partners during the past year:

Tracy – Last sexual exposure 3 weeks ago (receptive oral and vaginal sex with Stan)

Danielle – Last sexual exposure 6 weeks ago (vaginal sex with Stan)

Jonathan – Last sexual exposure 1 month ago (receptive anal sex with Stan)

Tony – Last sexual exposure 8 months ago (insertive oral and anal sex with Stan)

Carrie – Last sexual exposure 6 months ago (receptive oral and vaginal sex with Stan)

#### **8. Which of Stan's partners should be evaluated and treated prophylactically, even if their test results are negative?**

Tracy, Danielle, and Jonathan. Partners exposed to patients with primary syphilis within 90 days prior to the onset of symptoms may be infected even if seronegative.

Therefore, they should be treated presumptively. Tracy, Danielle, and Jonathan all had sex with Stan within the 90 days prior to the onset of his symptoms.

Partners exposed to patients with primary syphilis more than 90 days prior to the onset of symptoms are unlikely to be related to the infection.

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**9. Stan's partner, Tracy, is found to be infected and is diagnosed with primary syphilis. She is also in her second trimester of pregnancy and is allergic to penicillin. What is the appropriate treatment for Tracy?**

Pregnant women with syphilis who are skin-test-reactive to penicillin should be desensitized in the hospital and treated with penicillin. Penicillin is effective for preventing maternal transmission to the fetus and for treating fetal infection. Doxycycline is not appropriate for syphilis in pregnancy.

All patients who have syphilis should be offered testing for HIV infection.

Tracy should receive counseling about the risk of reinfection. Her serologic titer should be repeated at least in the third trimester and at delivery.

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**Follow-Up**

Stan returned to the clinic for a follow-up exam one week later. Results were as follows:

- His penile lesion was almost completely healed.
- He had not experienced a Jarisch-Herxheimer reaction.
- The RPR (repeated at the follow-up visit because the initial one was negative) was 1:2.

**10. What type of follow-up evaluation will Stan need?**

- Re-examine clinically and serologically at 6 and 12 months after therapy.
- Repeat the HIV antibody test at 3 months.

**11. What are appropriate prevention counseling messages for patients with syphilis?**

Correct responses may include any of the following:

Patient counseling and education should cover the nature of the disease, transmission, treatment and follow-up, and risk reduction.

Nature of the disease

- Syphilis may be symptomatic or asymptomatic.
- Because syphilis is a systemic infection, extra-genital symptoms (such as rashes and alopecia) may occur.
- Untreated syphilis in pregnancy can lead to death or severe disability in the fetus.
- Sequelae of untreated syphilis include neurologic and cardiovascular disorders

### Transmission

- Syphilis is transmitted sexually or vertically (from pregnant mother to fetus).
- Syphilis is most infectious during the primary and secondary stages (when lesions or rashes are present). However, lesions may be inapparent. **All at-risk sex partners** need to be evaluated and possibly treated.
- Syphilis is associated with increased susceptibility to HIV acquisition.

### Treatment and follow-up

- If treated with penicillin, the Jarisch-Herxheimer reaction may occur.
- Return for follow-up serology at 6 and 12 months (every 3 months if HIV-positive).
- The patient may be “serofast” or have positive treponemal and nontreponemal serologic tests for life.

### Risk reduction

The clinician should:

- Assess the patient’s potential for behavior change.
- Discuss prevention strategies such as abstinence, mutual monogamy with an uninfected partner, use of condoms, and limiting the number of sex partners.
- Discuss latex condoms, which when used consistently and correctly, can reduce the risk of syphilis transmission only when the infected area or site of potential exposure is protected. Genital ulcer diseases, including syphilis, can occur in male or female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered.
- Discuss individualized risk-reduction plans.

## TEST QUESTIONS

1. Which of the following contributed to the decrease in reported syphilis cases that began in the 1950s?
  - a) The end of World War II
  - b) The beginning of the Korean War
  - c) Use of penicillin to treat syphilis**
  - d) Decrease in syphilis surveillance efforts
2. At which stage of syphilis can neurosyphilis occur?
  - a) Primary syphilis
  - b) Secondary syphilis
  - c) Early latent syphilis
  - d) Latent syphilis of unknown duration
  - e) Any stage of disease**
3. A syphilis chancre can mimic which diseases?
  - a) Herpes and chancroid**
  - b) Chlamydia and herpes
  - c) PID and chlamydia
  - d) HPV and gonorrhea
4. What is the distinctive shape of *Treponema pallidum*?
  - a) Isosahedral-shaped
  - b) Corkscrew-shaped**
  - c) Ciliated body
  - d) Rod-shaped
5. To what values are follow-up titers compared?
  - a) CDC guideline standards
  - b) Nontreponemal titers obtained on the day of treatment**
  - c) Sex partner's titers
  - d) None of the above are correct
6. Rates of primary and secondary syphilis in the U.S. have declined every year since 1990.
  - a) True
  - b) False**
7. Which of the following are true about syphilis in the U.S.? (Mark all that apply)
  - a) Recent syphilis outbreaks have occurred in subpopulations of men who have sex with men (MSM).**
  - b) Reported cases of primary and secondary (P&S) syphilis reached an all-time low in 2000.**
  - c) P&S syphilis is widespread throughout the United States
  - d) Syphilis disproportionately affects African Americans.**

8. Which of the following is true about primary syphilis?
- a) A painful chancre occurs at the site of inoculation.
  - b) **The chancre is generally painless and resolves without treatment.**
  - c) Nontreponemal serologic tests are always positive.
  - d) Generalized lymphadenopathy is common.
9. Which of the following is **not** a sign of secondary syphilis?
- a) Alopecia
  - b) **Chancre at the site of inoculation**
  - c) Condylomata lata
  - d) Palmar/plantar rash
  - e) Papulosquamous rash
10. Mucocutaneous lesions are most commonly seen during which stage of syphilis?
- a) Primary
  - b) **Secondary**
  - c) Latent
  - d) Tertiary
11. Which of the following is true regarding treatment of a woman diagnosed with secondary syphilis in her 36<sup>th</sup> week of pregnancy?
- a) The recommended treatment is erythromycin 500 mg four times daily for 14 days.
  - b) Syphilis is not transmitted to the fetus so she does not have to worry about her baby.
  - c) She will get multiple shots and this will be adequate treatment for both she and the baby.
  - d) **She needs immediate treatment with penicillin and the baby will need treatment after birth.**
12. In pregnancy, the risk of transmission to the fetus is highest during which stage(s) of syphilis?
- a) **Primary and secondary**
  - b) Late latent
  - c) Early latent
  - d) The risk is the same regardless of the stage of disease.
13. Which of the following is true regarding the progression of syphilis?
- a) The most common clinical manifestation of primary syphilis is a chancre at the site of inoculation.
  - b) Mucocutaneous lesions may occur during secondary syphilis.
  - c) Tertiary syphilis is rare.
  - d) **All of the above are correct.**

14. A patient with no clinical signs or symptoms, a history of a palmar rash six months ago, and a positive serologic test for syphilis (positive nontreponemal test with a positive confirmatory treponemal test) fits the criteria for:
- Secondary syphilis
  - Late latent syphilis
  - Early latent syphilis**
  - None of the above.
15. Which of the following is true regarding the diagnosis of syphilis?
- A reactive RPR or VDRL is sufficient for diagnosis of syphilis.
  - The serofast reaction occurs when a nontreponemal test reaction is overwhelmed by antigen-antibody excess.
  - A reactive nontreponemal test should be confirmed by a treponemal test.**
  - VDRL and RPR results cannot be reported quantitatively.
16. Which of the following may cause a false-positive serologic test for syphilis?
- Autoimmune disease
  - Febrile illness
  - Drug abuse
  - All of the above.**
17. Which of the following are appropriate next steps in assessing a patient known only to have a “positive RPR”?
- Order a quantitative serologic nontreponemal test (e.g., RPR) and a confirmatory serologic treponemal test (e.g., FTA-ABS).
  - Obtain a detailed history and assess whether the patient has had syphilis before.
  - Contact your local health department STD program to see if they have additional information about the patient.
  - All of the above may be appropriate.**
18. The CDC-recommended treatment for primary syphilis without neurological involvement in an adult is:
- Benzathine penicillin G 7.2 million units IM in single dose
  - Benzathine penicillin G 7.2 million units IM in 3 divided doses
  - Benzathine penicillin G 2.4 million units in a single dose**
  - Doxycycline 100 mg orally daily for 14 days
19. The CDC-recommended treatment for tertiary syphilis without neurological involvement in an adult is:
- Benzathine penicillin G 7.2 million units administered as 3 doses each at 1-week intervals**
  - Benzathine penicillin G 7.2 million units administered as 1 dose
  - Doxycycline 100 mg orally twice daily for 14 days
  - Tetracycline 500 mg orally 4 times per day
20. The CDC-recommended therapy for a pregnant woman with early latent syphilis is:

- a) Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
  - b) **Benzathine penicillin G, IM, 2.4 million units in a single dose**
  - c) Erythromycin 500 mg orally 4 times a day for 14 days
  - d) Doxycycline 100 mg orally twice a day for 14 days
21. As part of the follow up for adult patients with syphilis (without HIV infection), quantitative VDRL or RPR should be repeated at \_\_\_ months after treatment?
- a) 3
  - b) **6**
  - c) 9
  - d) 12
22. Which of the following changes in titer should prompt concern about possible treatment failure or reinfection?
- a) Treatment date: RPR 1:128, six-month follow up: RPR 1:32
  - b) Treatment date: VDRL 1:128, six-month follow up: VDRL 1:16
  - c) **Treatment date: RPR 1:128; six-month follow up: RPR 1:64**
  - d) All of the above reflect adequate response to therapy.
23. Patients with syphilis should be advised that:
- a) The patient may be “serofast” or have positive treponemal and nontreponemal serologic tests for life.
  - b) All at-risk sex partners need to be evaluated and possibly treated for syphilis, even if they have not noticed symptoms.
  - c) Untreated syphilis can lead to serious sequelae, including neurologic and cardiovascular disorders.
  - d) **All of the above.**
24. Joey was diagnosed with primary syphilis and treated on April 15. At that time, he had a penile lesion that had been present for two weeks. He had three sex partners since the beginning of the year. Which of them should be treated presumptively?
- a) Frances (last exposure March 15)
  - b) Taylor (last exposure April 7)
  - c) Casey (last exposure February 14)
  - d) **All of them should be treated presumptively.**
25. Who is responsible for reporting a case of syphilis to the local health department?
- a) The laboratory
  - b) The health care provider
  - c) None of the above—syphilis is not reportable in most states.
  - d) **Depending on the state, the laboratory and/or the health care provider.**

## RESOURCES

### Publications

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### Websites and Other Resources

1. CDC, Division of STD Prevention: [www.cdc.gov/std](http://www.cdc.gov/std)
2. National Network of STD/HIV Prevention Training Centers: <http://depts.washington.edu/nnptc/>
3. Syphilis Algorithms from the California STD/HIV Prevention Training Center: <http://www.stdhivtraining.org/cfm/resources.cfm#SyphilisTools>
4. 2002 CDC STD Treatment Guidelines (including downloadable version for Palm devices): <http://www.cdc.gov/STD/treatment/>
5. CDC National STD Hotline: 800-227-8922 or 800-342-2437
  - a. En Español: 800-344-7432
  - b. TTY for the Deaf and Hard of Hearing: 800-243-7889
6. CDC National Prevention Information Network (NPIN): [www.cdcpin.org](http://www.cdcpin.org)
7. American Social Health Association (ASHA): [www.ashastd.org](http://www.ashastd.org)