Syphilis

DESCRIPTION

Syphilis is a systemic disease caused by *Treponema pallidum*, a spirochete with characteristic spirals and motility. It is usually acquired by sexual contact, but it may also be passed from mother to fetus. Syphilis is divided into early and late stages. Early syphilis is further divided into an incubation period, primary, secondary and early latent stages. CNS involvement can occur during any stage of syphilis.

SYMPTOMS

Primary Infection:

- Ulcer(s) or chancre(s) at site of infection

Lesion appears 2-12 weeks (usually 3 weeks) after contact at site of exposure to the infected lesions of another person; may persist for 1-5 weeks then resolves.

Secondary Infection:

- Symmetrical rash, often on the palms of hands, bottom of feet, on the torso, or other sites
- Mucus patches in oral cavity or vagina
- Condylomata lata, flat wart-like growths, in the perianal/genital area and other moist body sites
- Generalized lymphadenopathy
- Alopecia

Onset of symptoms typically occurs 6 weeks to 6 months after onset of the chancre (can overlap with primary) and resolves in 2-10 weeks. 25% may have relapses of signs and symptoms in first year.

CASE REPORTING

Both providers and labs are required to complete a Case Report Card.

Case Report Cards must be submitted within one working day, via:

- confidential fax: 651-201-4040
- mail to:
  IDEPC
  Minnesota Department of Health
  625 Robert Street N.
  P.O. Box 64975
  St. Paul, MN 55164-9703
- or by phone to Syphilis Surveillance at 651-201-4024

Case Report Cards are available by calling 651-201-5414 or 877-676-5414

Latent Syphilis:

Latent syphilis is defined as seroreactivity without other evidence of disease.

- Patients who have latent syphilis and who acquired syphilis within the preceding year are classified as having early latent syphilis.
- The majority of people with latent syphilis may be asymptomatic for many years.

Tertiary Syphilis:

Tertiary syphilis is defined as symptomatic late syphilis, gumma and cardiovascular syphilis, but not all neurosyphilis.

- Organ damage, including the heart, blood vessels, liver, bones, and joints
- Gummatous lesions

Neurosyphilis:

CNS involvement can occur during any stage of syphilis.

- Cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis
- Uveitis or other ocular manifestations

RISK FACTORS

- Exposure to syphilis
- Other new STD diagnosis
- HIV infected
- Men who have sex with men
- Sexual partners of men who have sex with men
- Exchanges sex for drugs or money or having partners who do
- Multiple sex partners (based on history and clinician discretion)
- Sexual assault

Routine Screening is recommended:

- On at least an annual basis for all men who have sex with men, and more often for those at higher risk
- For individuals with multiple sex partners in the last year
- For pregnant women at their first prenatal visit, plus, for those at high risk, at 28 weeks gestation and at delivery

EXAMINATION

- Identification of *T. pallidum* through darkfield examination or direct fluorescent antibody tests of lesion, exudate, or tissue is definitive for diagnosis of early syphilis.

Serology:

Both a nontreponemal and treponemal test should be performed, with the nontreponemal as a quantitative measure and the treponemal to confirm, as part of diagnostic steps.

- Nontreponemal screening (USR, VDRL, or RPR):
  - Non-treponemal antibody titers often correlate with disease activity, and results should be reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g. 1:16 from 1:4), is necessary to demonstrate a substantial difference between two nontreponemal test results that were obtained using the same serologic test.
  - Nontreponemal tests usually will become non-reactive with time after treatment; however in some patients non-treponemal antibodies can persist at low titer for a long time, sometimes for the life of the patient. Therefore, if available, it is important to compare previous test results to a more recent nontreponemal results as described above, to aid in diagnosing re-infection.
  - Nontreponemal test results should be confirmed with a treponemal test.
  - Possible causes of acute and chronic false positive reactions in nontreponemal serology:

Acute		Chronic
Hepatitis	Mononucleosis	Lupus
Viral pneumonia	Chicken pox	Immunoglobulin abnormalities
Measles	Viral infections	Narcotic addiction
Malaria	Immunizations	Aging
Pregnancy	Drug use	Leprosy
	Technical error	Malignancy

- Treponemal (FTA-ABS, TTPA, or MHA-TP):
  - Patients with reactive treponemal tests will usually have a reactive test result for a lifetime.
  - Patients with a documented negative syphilis serology within the past year who present with positive serology are classified as having early syphilis.
  - Treponemal test is done:
    - To confirm nontreponemal reactive results
    - At recent onset of suspicious new lesion

Cerebrospinal Fluid (CSF) Exam:

- Recommended for suspected tertiary syphilis or neurosyphilis, latent syphilis with treatment failure, or late-latent or of unknown duration for those HIV infected. Some clinicians recommend CSF examination for other indications, also. See 2006 CDC treatment guidelines, pg.26.
- VDRL test on CSF is highly specific but not sensitive
- FTA-ABS test on CSF is less specific but highly sensitive and some specialists use to exclude neurosyphilis

Considerations:

- Any history of biological false positive test (BFP)
- History of yaws or pinta
- History of previous serologies including plasma and blood donation
- History of previous infection:
  - Asking when and where treated
  - Stage of disease treated
  - Medication and dosage used in treatment

DIAGNOSTIC CRITERIA

Primary Syphilis:

- Genital lesion at time of examination with positive darkfield examination or reactive nontreponemal and treponemal serologies
- Unequivocal symptoms of primary syphilis at time of examination with known exposure, regardless of serology

Secondary Syphilis:

- Presence of secondary syphilis symptoms at time of examination and reactive nontreponemal and treponemal serologies

Early Latent Syphilis:

- Fourfold or greater increase in nontreponemal test titer in the previous 12 months
- Unequivocal history of symptoms of primary or secondary syphilis in the previous 12 months
- A sex partner in the last year documented to have primary, secondary, or early latent syphilis
- Reactive nontreponemal and treponemal tests in a person whose only possible exposure occurred within the previous 12 months

Late Latent Syphilis:

- No clinical signs of primary or secondary syphilis currently or within the past year
- No documentation of conversion from non-reactive to reactive in previous year
- If no prior syphilis serology is documented, repeat serology in one week—if no increase in titer, diagnose as late latent syphilis and begin treatment
  - Initiation of treatment may begin at the time of the second blood draw
  - Further treatment will be determined by second serology test results
- Evaluate for evidence of tertiary symptoms (e.g. aortitis, gumma, iritis)

Neurosyphilis:

- No single test can be used to diagnose neurosyphilis
- Reactive VDRL from CSF (see Cerebrospinal Fluid [CSF] exam, pg. 2)
- Evaluate for evidence of neurosyphilis symptoms (e.g., cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms of meningitis).

Tertiary Syphilis:

- If tertiary syphilis is suspected, consult with infectious disease specialist. See the 2006 CDC treatment guidelines (pg 27).

Other Considerations:

- Sequential serological tests in individual patients should be performed using the same testing method because different quantitative tests cannot be compared directly.
- All patients with syphilis should be tested for HIV.
- Differential Diagnosis:
  - Primary: chancroid, trauma, fixed drug eruption, lymphogranuloma venereum, herpes
  - Secondary: pityriasis rosea, erythema multiforme, psoriasis, numular eczema, drug eruption

TREATMENT

Primary, Secondary and Early Latent:

- Non-penicillin allergic: benzathine penicillin G (BICILLIN L-A) I 2.4 million units M once. (Note: Bicillin C-R should **NOT** be used to treat syphilis) Advise patient regarding possible Jarisch-Herxheimer reaction
- Penicillin allergic: doxycycline 100 mg B.I.D. x 14 days or tetracycline 500 mg Q.I.D. x 14 days

Late Latent (infection of more than 1 year or of unknown duration) Syphilis and Tertiary Syphilis:

- Non-penicillin allergic: benzathine penicillin G (BICILLIN L-A) 2.4 million units IM every week for 3 weeks. (Note: Bicillin C-R should **NOT** be used to treat syphilis.) Advise patient regarding possible Jarisch-Herxheimer reaction.
- Penicillin allergic: doxycycline 100 mg B.I.D. x 28 days or tetracycline 500 mg Q.I.D. x 28 days

Neurosyphilis:

- Aqueous crystalline penicillin G 18-24 million units administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days
- Penicillin allergic: ceftriaxone has been used by some clinicians. See the 2006 the CDC treatment guidelines (pg. 28)

Other Considerations:

- Offer HIV testing.

Special Populations:

- HIV infected patients
  - Treatment regimen may be the same as for non-HIV infected patients, however, some specialists recommend benzathine penicillin (BICILLIN L-A) 2.4 million units IM every week for 3 weeks for early syphilis. Consult your medical director.
- Pregnant women with penicillin allergies
  - See 2006 the CDC treatment guidelines (pg. 29-32) regarding treatment and follow-up, including follow-up for the newborn. No proven alternatives exist for pregnant women with a history of allergy. Patient should be desensitized and treated with the penicillin regiment appropriate to the stage of syphilis.
- Infants
  - See 2006 the CDC treatment guidelines (pg. 30-33)

FOLLOW UP

- Primary and secondary syphilis, examine clinically 6 months and 12 months after treatment (3, 6, 9, 12, and 24 months for those HIV infected) and serologically.
- Latent syphilis, examine serologically 6, 12, and 24 months after treatment (6, 12, 18, and 24 months for those HIV infected).
- Tertiary syphilis should be managed in consultation with infectious disease specialist. See the 2006 CDC treatment guidelines, (pg. 27).
- For neurosyphilis, see the 2006 CDC treatment guidelines, (pg. 28).

Re-treat if:

- Titer increases fourfold or initially high titer (1:32 or higher) fails to decline at least fourfold in 6 months or remains serofast, or symptoms persist or reoccur.

Re-treatment:

- Benzathine penicillin G (BICILLIN L-A) 2.4 million units IM every week for 3 weeks, unless CSF exam indicated neurosyphilis is present

Other Considerations:

- Re-evaluate for HIV infection, if needed.
- CSF examination is often recommended for all stages of treatment failure.

MANAGEMENT OF PARTNERS

Partners of patients with syphilis should receive:

- Routine history
- Examination
- Syphilis serology (nontreponemal test)
- Treatment, if they had sexual contact with the patient within the preceding 90 days and:
  - the index patient has been diagnosed with primary, secondary, or early latent syphilis, or
  - with syphilis of unknown duration with a high nontreponemal serologic test titers (i.e. >=1:32).
- Treatment, if they had sexual contact with the patient more than 90 days previous if serological tests are not immediately available and follow-up is uncertain.

Advise HIV testing for all partners as needed.