BACTERIAL STDS

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Chlamydia (CT)

Urethral CT

Symptoms

Urethral CT is often asymptomatic. Symptoms, if present, may be mild and include discharge and/or dysuria. Symptoms typically occur 7-21 days after exposure. Discharge, if present, is typically clear and mucoid.

Diagnostic testing

NAAT on urine specimens is the recommended testing method.

Treatment

Recommended Regimens

- Azithromycin 1 g orally in a single dose, OR
- Doxycycline 100 mg orally twice a day for 7 days

Alternative Regimens

- Erythromycin base 500 mg orally four times a day for 7 days, OR
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days, OR
- Levofloxacin 500 mg orally once daily for 7 days, OR
- Ofloxacin 300 mg orally twice a day for 7 days

Follow-Up

CT-infected men should be retested approximately 3 months after treatment to assess for repeat infection. Retesting can be performed opportunistically any time between 1-12 months post-treatment and should be performed regardless of whether the patient believes that their partners were treated.[43] Retesting is different from a test of cure (TOC), which is typically performed to rule out treatment failure. TOC is not routinely recommended for CT.

[43] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/chlamydia.htm

Anorectal CT

Symptoms

Anorectal CT is usually asymptomatic (86%), except for CT strains associated with lymphogranuloma venereum (LGV) [44], which often produce symptomatic proctocolitis. Symptoms may include rectal pain, discharge, bleeding, constipation, tenesmus and fever. Abnormal anoscopic findings include mucopurulent discharge, mucosal erythema, and easily induced mucosal bleeding.

Diagnostic testing

- NAAT performed on rectal swabs is preferred. All commonly available NAATs identify both LGV and non-LGV serovars of CT, but do not differentiate specific serovars. A positive NAAT for CT in a patient with symptoms of proctocolitis supports diagnosis of LGV.
- Culture, if NAAT unavailable. Culture is less sensitive than NAAT.
- Serology is not useful to support a diagnosis of rectal LGV.
- Currently available diagnostics for LGV are limited, therefore healthcare providers must make a clinical decision regarding whether to treat empirically for LGV. Presumptive treatment of LGV is recommended for MSM with proctitis and anorectal CT, particularly if the patient is HIV-infected or if symptoms such as bloody discharge, perianal ulcers, or mucosal ulceration are present.

Treatment

Recommended Regimens (low suspicion for LGV)

- Azithromycin 1 g orally in a single dose, OR
- Doxycycline 100 mg orally twice a day for 7 days

Alternative Regimens (low suspicion for LGV)

- Erythromycin base 500 mg orally four times a day for 7 days, OR
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days, OR
- Levofloxacin 500 mg orally once daily for 7 days, OR
- Ofloxacin 300 mg orally twice a day for 7 days

Recommended Regimens (high suspicion for LGV)

- Doxycycline 100 mg orally twice a day for 21 days

Alternative Regimen (high suspicion for LGV)

- Erythromycin base 500 mg orally four times a day for 21 days

Follow-Up

Symptomatic patients should be followed clinically until signs and symptoms have resolved. All CT-infected men should be retested approximately 3 months after treatment to assess for repeat infection. Retesting can be performed opportunistically any time between 1-12 months post-treatment and should be performed regardless of whether the patient believes that their partners were treated.[45] Retesting is different from a TOC, which is typically performed to rule out treatment failure. TOC is not routinely recommended for CT.

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[44] LGV is a systemic STD caused by CT serovars L1, L2 or L3 affecting lymph nodes & rectum. For more information, please refer to the 2015 STD Treatment Guidelines.

[45] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/chlamydia.htm

Pharyngeal CT

Symptoms

Pharyngeal CT is usually asymptomatic and infections are not common among MSM, as the pharynx is not a hospitable environment for CT. As a result, pharyngeal CT screening for MSM is not specifically recommended by the CDC.

Diagnostic laboratory testing

Testing for pharyngeal CT is not recommended. However, most NAATs combine testing for CT and GC. If pharyngeal CT is identified, treat per recommendations.

Treatment

Recommended Regimens

- Azithromycin 1 g orally in a single dose, OR
- Doxycycline 100 mg orally twice a day for 7 days

Alternative Regimens

- Erythromycin base 500 mg orally four times a day for 7 days, OR
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days, OR
- Levofloxacin 500 mg orally once daily for 7 days, OR
- Ofloxacin 300 mg orally twice a day for 7 days

Follow-Up

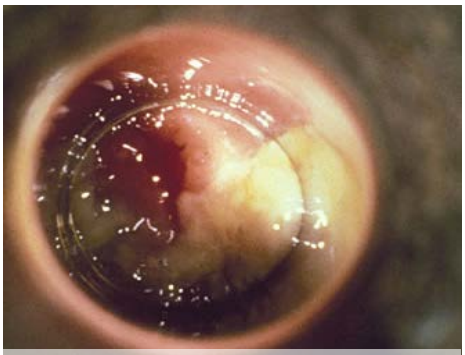
CT-infected men should be retested approximately 3 months after treatment to assess for repeat infection. Retesting can be performed opportunistically any time between 1-12 months post-treatment and should be performed regardless of whether the patient believes that their partners were treated.[46] Retesting is different from a TOC, which is typically performed to rule out treatment failure. TOC is not routinely recommended for CT.

[46] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/chlamydia.htm

Figure 7. Clinical manifestations of CT

Seattle STD/HIV Prevention Training Center
Source: University of Washington

Nongonococcal urethritis.



Seattle STD/HIV Prevention Training Center
Source: Connie Celum; Walter Stamm

LGV proctitis with mucupurulent discharge.

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LGV primary lesion.

Gonorrhea (GC)

Urethral GC

Symptoms

Urethral GC can be asymptomatic in men (10-20%). Typically onset is abrupt with purulent urethral discharge often accompanied by severe dysuria, but discharge may be clear or cloudy, and mild dysuria can also occur. Onset of symptoms is about 2-10 days after exposure.

Diagnostic laboratory testing

- NAAT performed on urine specimens are the recommended testing method. If NAATs are unavailable, culture may be performed.
- Both culture and NAAT should be performed if there is suspicion for treatment failure due to a resistant strain of *N. gonorrhoeae.* Antimicrobial susceptibility testing should also be requested if culture is performed.
- Gram stain of urethral discharge can be used for symptomatic patients (sensitivity and specificity >95%), but is less sensitive in asymptomatic patients (50%).The presence of Gram negative intracellular diplococci (GNID) is diagnostic of GC.

Treatment

Recommended Regimen

Dual therapy administered concurrently with

- Ceftriaxone 250 mg in a single intramuscular (IM) dose **PLUS** Azithromycin 1 g orally in a single dose (*preferred)*

Alternative Regimens, if ceftriaxone is unavailable

Dual therapy administered concurrently with

- Cefixime 400 mg in a single oral dose **PLUS** Azithromycin 1 g orally in a single dose *(preferred)*

If the patient has cephalosporin allergy or history of severe allergy to penicillin:
Dual therapy administered concurrently with

- Gemifloxacin 320 mg in a single oral dose **PLUS** Azithromycin 2 g orally in a single dose, OR
- Gentamicin 240 mg in a single IM dose **PLUS** Azithromycin 2 g orally in a single dose

Follow-Up

GC-infected men should be retested approximately 3 months after treatment to assess for repeat infection, regardless of whether they believe that their partners were treated.[47] Retesting is different from a TOC, which is typically performed to rule out treatment failure. TOC is not routinely recommended for urethral GC.

[47] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/gonorrhea.htm

Rectal GC

Symptoms

Rectal GC is mostly asymptomatic (more than 90%). When symptoms occur, they may include proctitis, anal irritation, painful defecation, constipation, rectal bleeding and/or discharge, and tenesmus. Anoscopic findings include mucopurulent discharge, mucosal erythema and easily induced mucosal bleeding.

Diagnostic laboratory testing

- NAAT performed on rectal swabs is the preferred testing method. Specimens must be sent to a laboratory that has established performance specifications for performing NAATs on rectal swabs.[48]

Treatment

Recommended Regimen

Dual therapy administered concurrently with

- Ceftriaxone 250 mg in a single intramuscular (IM) dose **PLUS** Azithromycin 1 g orally in a single dose (*preferred)*

Alternative Regimens, if ceftriaxone is unavailable

Dual therapy administered concurrently with

- Cefixime 400 mg in a single oral dose **PLUS** Azithromycin 1 g orally in a single dose *(preferred)*

If the patient has cephalosporin allergy or history of severe allergy to penicillin:

Dual therapy administered concurrently with

- Gemifloxacin 320 mg in a single oral dose **PLUS** Azithromycin 2 g orally in a single dose, OR
- Gentamicin 240 mg in a single IM dose **PLUS** Azithromycin 2 g orally in a single dose

Follow-Up

GC-infected men should be retested approximately 3 months after treatment to assess for repeat infection, regardless of whether they believe that their partners were treated.[49] Retesting is different from a TOC, which is typically performed to rule out treatment failure. TOC is not routinely recommended for rectal GC.

[48] For more information on NAATs in rectal and pharyngeal specimens contact the Health Department or visit the Association of Public Health Laboratories guidance for non-FDA cleared tests at the following links: Rectal swabs: www.cdph.ca.gov/programs/std/Documents/NAATRectalSwabs.pdf Pharyngeal swabs: www.aphl.org/aphlprograms/infectious/std/Documents/NAATThroatSwabs.pdf. A list of national labs that accept these specimens is available at www.aphl.org/aphlprograms/infectious/Archive/naatestlabs.aspx

[49] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/gonorrhea.htm

Pharyngeal GC

Symptoms

Pharyngeal GC is mostly asymptomatic (~90%). Signs and symptoms that occur are similar to other causes of pharyngitis.

Diagnostic laboratory testing

- NAAT performed on pharyngeal swab is the preferred testing method. Specimens must be sent to a laboratory that has established performance specifications for performing NAATs on pharyngeal swabs.[48]
- Culture, if NAAT unavailable. Culture is less sensitive and requires use of selective media and environmental conditions that support the growth of *N. gonorrhoeae*.

Treatment

Recommended Regimen

Dual therapy administered concurrently with

- Ceftriaxone 250 mg in a single IM dose **PLUS** Azithromycin 1 g orally in a single dose

Follow-Up

GC-infected men should be retested approximately 3 months after treatment to assess for repeat infection, regardless of whether they believe that their partners were treated.[50]

The CDC also recommends patients treated with an alternative regimen for pharyngeal GC receive a TOC in 14 days using either culture or NAAT. If NAAT is positive, effort should be made to perform a confirmatory culture before retreatment. All positive TOC cultures should undergo antimicrobial susceptibility testing.

Symptoms that persist after treatment should be evaluated by culture for GC and undergo antimicrobial susceptibility testing.

[50] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/gonorrhea.htm

Figure 8. Clinical manifestations of GC

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Urethral GC

Special Considerations for Suspected GC Treatment Failure

Recommendations for management of suspected GC treatment failure may change. Please refer to the California Gonorrhea Treatment Guidelines for Suspected Gonorrhea Treatment Failure[51] for the most updated information.

Treatment failure should be suspected if symptoms persist or recur following initial antibiotic therapy.

Figure 9: Symptoms of potential GC treatment failure by site of infection

Original site of infection	Potential treatment failure symptoms
Urethra	Discharge, dysuria, pyuria (leukocyte esterase on urine dipstick, or ≥ 10 white blood cells (WBC) per high power field on microscopy of urine sediment)
Pharynx	Pharyngitis or odynophagia
Rectum	Discharge, pain, bleeding, pruritis, tenesmus, or painful defecation

Prepared by the California Department of Public Health

For patients with suspected treatment failure, the following steps should be taken to ensure adequate testing, treatment, partner management, and follow up:

- Obtain specimens for NAAT and culture at sites of sexual exposure (i.e., genital, rectal, pharyngeal). If GC culture is not available at your local laboratory, contact the CDPH STD Control Branch clinician warm line at (510) 620-3400, Monday-Friday, 8am-5pm for assistance.
- Treat with either: 1) Gentamicin 240 mg IM **PLUS** Azithromycin 2 g orally, or 2) Gemifloxacin 320 mg orally **PLUS** Azithromycin 2 g orally.
- Report the case to your local health department within 24 hours. Please also call the CDPH STD Control Branch clinician warm line at (510) 620-3400.
- Ensure that all of the patient's partners in the last 60 days are notified and referred for testing and empiric treatment with the same regimen used to treat the index patient. Your local health department should be able to provide assistance with partner notification.
- Instruct the patient to abstain from oral, vaginal, and anal sex until one week after the patient and all of his/her partners are treated and all symptoms have resolved.
- Ensure that the patient returns in 7-14 days for a TOC with culture and NAAT.

[51] www.cdph.ca.gov/pubsforms/Guidelines/Pages/CAGuidelinesGonorrheaTxFailure.aspx

Note: Susceptibility testing should be performed for gonococcal isolates found on a positive TOC culture, including cephalosporin, macrolide, tetracycline, and fluoroquinolone susceptibility. If local susceptibility testing is performed, the specimen (or aliquot of the specimen) should be preserved for future analysis in the event that decreased susceptibility is identified.

The above recommendations are meant for patients with treatment failure after dual therapy with ceftriaxone plus azithromycin. Patients with persistent symptoms or a positive TOC after treatment with a non-recommended regimen (e.g. fluoroquinolones) should be treated with ceftriaxone 250 mg IM plus azithromycin 1g orally. For patients with treatment failure after azithromycin monotherapy, call the CDPH STD Control Branch clinician warm line for consultation.

If patient is allergic to ceftriaxone then additional therapies that can be considered include 1) gentamicin 240 mg IM plus azithromycin 2 g orally in a single dose or 2) gemifloxacin 320 mg orally in a single dose plus azithromycin 2 g orally in a single dose.

Reinfection should be suspected in a patient who reports interim sexual exposure to untreated or new sex partners. Patients with suspected reinfection should be treated with ceftriaxone 250 mg IM plus azithromycin 1 g orally. Providers do not need to inform the local health department for suspected reinfection cases.

For assistance or clinical consultation regarding patients with ongoing treatment failure, patients with severe allergies, or other challenging cases, please call the CDPH STD Control Branch clinician warm line at (510) 620-3400, 8 am – 5 pm, Monday – Friday and ask to speak with the clinician on call. For more information about STDs, please visit the CDPH STD Control Branch webpage: www.std.ca.gov.

Syphilis

Primary Syphilis

Symptoms

Primary syphilis is symptomatic, though ulcers may go unnoticed by patients. Lesions appear 10-90 days (average 3 weeks) after contact at the site of exposure, persist for days to weeks, and resolve without treatment. Typical lesions are single, painless, indurated, clean based ulcers. Atypical lesions can mimic herpes and other genital ulcers.

HIV-infected patients are more likely to have persistent lesions into the secondary stage, and are more likely to present with atypical lesions (40% compared to 25% in HIV-uninfected patients).

Further testing is warranted for persons with clinical signs of neurosyphilis (e.g., cranial nerve dysfunction, auditory or ophthalmic abnormalities, meningitis, stroke, acute or chronic altered mental status, and loss of vibration sense).[52]

Neurosyphilis can occur during any stage of syphilis (see *Neurosyphilis* on page 52).

Diagnostic Laboratory Testing

- Darkfield microscopy on exudate of lesion is the recommended point-of-care test, though it is not widely available. Sensitivity ranges between 80-90% and varies with time of processing, skill of examiner, and age of the lesion.
- STAT RPR can be performed to assist in diagnosis. If not available and high suspicion for syphilis exists, treat presumptively as described below.
- Simultaneous serologic testing for non-treponemal (RPR/VDRL) and treponemal (TP-PA/FTA-ABS/EIA/CIA) tests are recommended, as treponemal tests may become reactive sooner than non-treponemal tests in primary syphilis.[53] A negative RPR/VDRL does not exclude the diagnosis of primary syphilis. Reactive RPR/VDRL tests should be quantified for serologic follow up.

Treatment

Recommended Regimens

- Benzathine penicillin G 2.4 million units IM in a single dose[54]

Alternative Regimens

- Doxycycline 100 mg orally twice daily for 14 days, OR
- Tetracycline 500 mg orally four times daily for 14 days, OR
- Ceftriaxone 1 g IM or intravenous (IV) once daily for 10-14 days

Counsel MSM about the possibility of a Jarisch-Herxheimer reaction, an acute febrile reaction frequently accompanied by headache, myalgias, fever, and other symptoms that usually occurs within the first 24 hours after the initiation of any therapy for syphilis. This reaction does not indicate allergy to antibiotic therapy. Over-the-counter nonsteroidal anti-inflammatory medications may be taken for symptomatic relief.

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[52] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/syphilis.htm

[53] Most patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity.

[54] Available data demonstrate that additional doses do not enhance efficacy when used to treat primary and secondary syphilis, regardless of HIV status.

Follow-Up

MSM should be re-evaluated one to two weeks following treatment for improvement of clinical symptoms and signs. Any symptoms of the Jarisch-Herxheimer reaction can be documented at this time.

Follow-up Titers

HIV-negative patients should receive quantitative RPR/VDRL tests at 6 and 12 months. HIV-infected patients should be evaluated clinically and serologically at 3, 6, 9, 12, and 24 months.

Successful Serologic Response

Serologic response to treatment is defined as a four-fold (or two-dilutional) decrease in the follow-up test titer in comparison to the titer obtained on the day of treatment (e.g., 1:128 to 1:32), over the 6 to 12 month period following treatment.

Serofast State

A persistent, low-level positive non-treponemal test titer (typically ≤1:8) is considered 'serofast', and has been found to occur more frequently in HIV-infected patients with syphilis. In the absence of a sustained (greater than 2 weeks) 4-fold rise in titer and/or re-emergence of symptoms and signs following treatment, such persons should be followed at least annually with clinical evaluation, risk assessment, and repeat serology to assess the need for repeat treatment, and lumbar puncture should be performed if neurologic signs or symptoms emerge.

Treatment Failure

Consider treatment failure in patients with persistent or recurring signs or symptoms, or who have a sustained fourfold increase in RPR/VDRL test titer (i.e., compared with the maximum or baseline titer at the time of treatment). Patients with suspected treatment failure should be retreated and a CSF analysis performed to assess for neurosyphilis. Patients should be treated with weekly injections of benzathine penicillin G 2.4 million units IM for 3 weeks unless CSF examination indicates that neurosyphilis is present, in which case treatment for neurosyphilis should be initiated (see *Neurosyphilis* on page 52).

Figure 10. Clinical manifestations of primary syphilis

San Francisco City Clinic, Source: Dr. Joseph Engelman

Typical chancre/sore – rubber edges, non-tender.

San Francisco City Clinic, Source: Dr. Joseph Engelman

Unusual shallow, multiple chancres/sores mimicking genital herpes.

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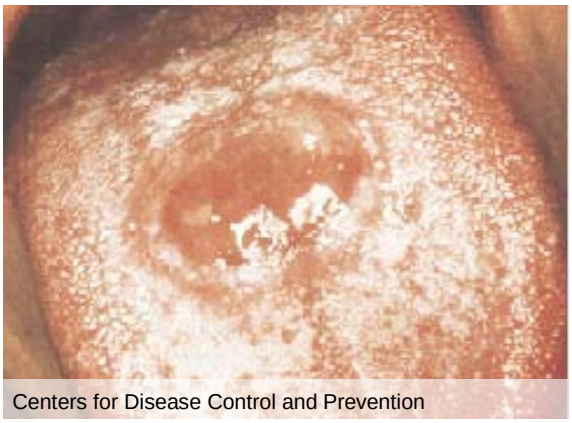
Multiple penile ulcers.

California STD Control Branch

Anal chancre.



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Tongue ulcer.

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Healing ulcer.

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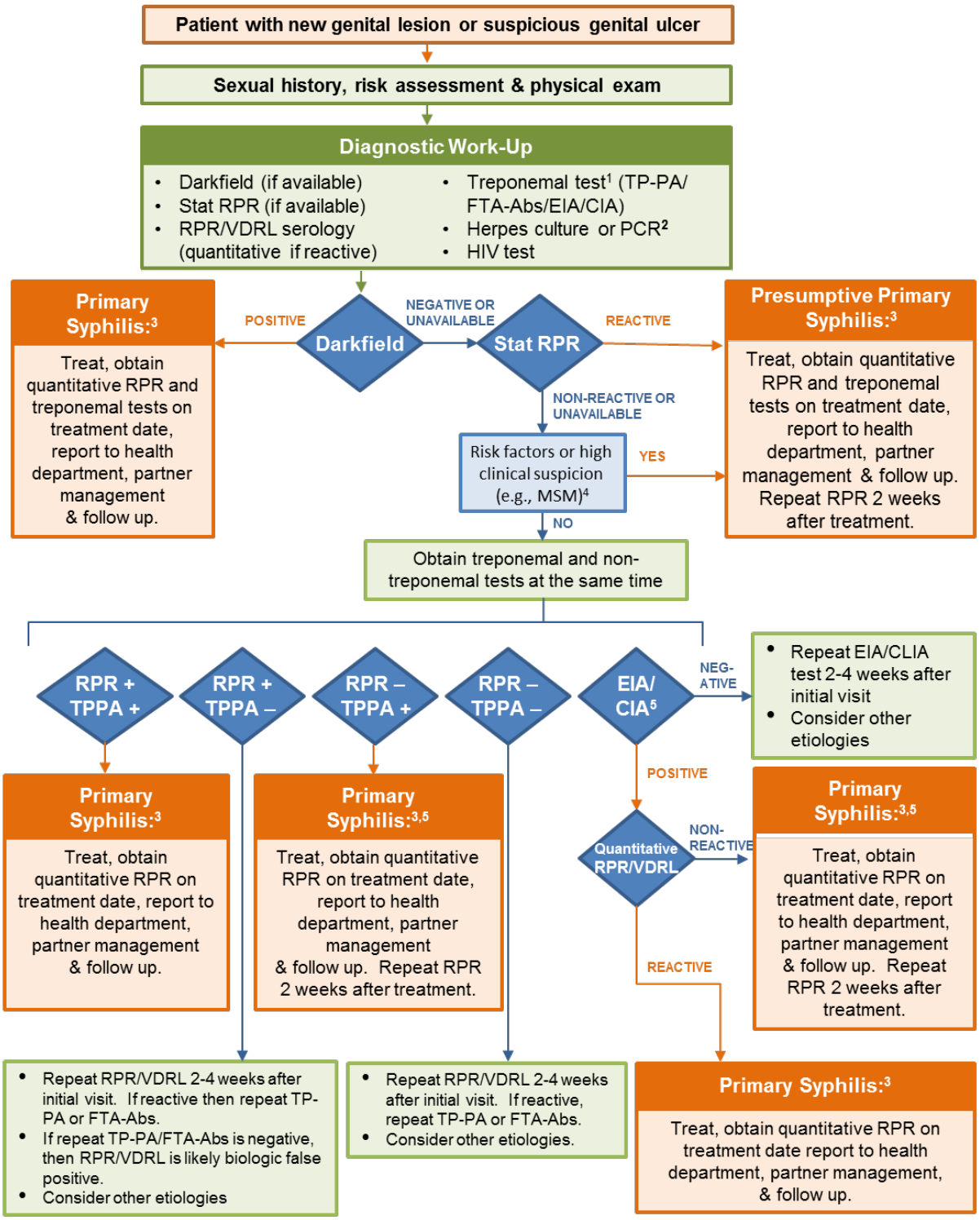
Figure 11. Algorithm for evaluating patients for primary syphilis



Prepared by the California Department of Public Health

[1] Treponemal tests may be more sensitive than non-treponemal tests during primary syphilis.
[2] Also consider culture for *Haemophilus ducreyi* (chancroid) if exposure in endemic areas or if lesion does not respond to syphilis treatment.
[3] All patients with suspected syphilis should be tested for HIV infection and screened for other STDs. Repeat HIV testing of patients with primary syphilis 3 months after the first HIV test, if the first test is negative.
[4] If the patient is MSM or has high risk sexual behavior or clinical exam with classic features of a syphilitic ulcer, then standard of care includes presumptive treatment at the time of the initial visit before diagnostic tests are available. Presumptive treatment is also recommended if patient follow-up is a concern.
[5] If the patient does not respond to treatment, repeat RPR/VDRL after treatment and consider other etiologies.

Secondary Syphilis

Symptoms

Signs and symptoms typically occur 3-6 weeks after the primary stage and resolve within 2-10 weeks without treatment, with 15% of patients experiencing relapses of signs and symptoms in the first year.

Signs and symptoms are variable and include:

- Rash (75-90%), which is usually nonpruritic and may involve the palms and soles (60%). A secondary syphilis rash may be widespread or localized, florid or subtle, and can be one or more of the following:
    - Macular (flat)
    - Papular (raised)
    - Squamous (scaly)
    - Pustular (occurs rarely)
    - Annular (occurs rarely)
- Generalized lymphadenopathy (70-90%) most commonly affects the inguinal, axillary and cervical sites.
- Constitutional symptoms (50-80%) include malaise and fever.
- Mucous patches (5-25%) are characterized as flat gray-white patches on the mucous membrane in the oral cavity and genital area.
- Condylomata lata (5-25%) are moist, heaped, wart-like lesions in genital, peri-rectal and rectal areas, and the oral cavity.
- Alopecia (10-15%) is characterized by patchy or moth-eaten hair loss and/or loss of lateral eyebrows.
- Neurosyphilis can occur during any stage of syphilis (see *Neurosyphilis* on page 52).

Diagnostic Laboratory Testing

- STAT RPR can be performed to assist in diagnosis. If not available and high suspicion for syphilis exists, treat presumptively as described below.
- Non-treponemal (RPR/VDRL) serologic testing is recommended, with reflex to treponemal (TP-PA/FTA-ABS/EIA/CIA) testing to confirm syphilis if positive. Non-treponemal tests should be quantified for serologic follow up.[55] If patient has signs or symptoms consistent with secondary syphilis but the RPR/VDRL is negative, request the lab dilute serum to at least 1:16 to rule out a prozone reaction.[56]

Treatment

Recommended Regimens

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

Alternative Regimens

- Doxycycline 100 mg orally twice daily for 14 days, OR
- Tetracycline 500 mg orally four times daily for 14 days, OR
- Ceftriaxone 1 g IM or IV once daily for 10-14 days

[55] Most patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity.

[56] The prozone reaction occurs in 1% of secondary syphilis cases, and is defined as a false negative non-treponemal test due to excess antibody blocking the antigen-antibody reaction.

Counsel patient about the possibility of a Jarisch-Herxheimer reaction, an acute febrile reaction frequently accompanied by headache, myalgias, fever, and other symptoms that usually occurs within the first 24 hours after the initiation of any therapy for syphilis. This reaction does not indicate allergy to antibiotic therapy. Over-the-counter nonsteroidal anti-inflammatory medications may be taken for symptomatic relief.

Follow-Up

MSM should be re-evaluated one to two weeks following treatment for improvement of clinical symptoms and signs. Any symptoms of the Jarisch-Herxheimer reaction can be documented at this time.

Follow-up Titers

HIV-negative patients should receive quantitative RPR/VDRL tests at 6 and 12 months. HIV-infected patients should be evaluated clinically and serologically at 3, 6, 9, 12, and 24 months.

Successful Serologic Response

Serologic response to treatment is defined as a four-fold (or two-dilutional) decrease in the follow-up test titer in comparison to the titer obtained on the day of treatment (e.g., 1:128 to 1:32), over the 6 to 12 month period following treatment.

Serofast State

A persistent, low-level positive non-treponemal test titer (typically ≤1:8) is considered 'serofast', and has been found to occur more frequently in HIV-infected patients with syphilis. In the absence of a sustained (greater than 2 weeks) 4-fold rise in titer and/or re-emergence of symptoms and signs following treatment, such persons should be followed at least annually with clinical evaluation, risk assessment, and repeat serology to assess the need for repeat treatment, and lumbar puncture should be performed if neurologic signs or symptoms emerge.

Treatment Failure

Consider treatment failure in patients with persistent or recurring signs or symptoms, or who have a sustained fourfold increase in RPR/VDRL test titer (i.e., compared with the maximum or baseline titer at the time of treatment). Patients with suspected treatment failure should be retreated and a CSF analysis performed to assess for neurosyphilis. Patients should be treated with weekly injections of benzathine penicillin G 2.4 million units IM for 3 weeks unless CSF examination indicates that neurosyphilis is present, in which case treatment for neurosyphilis should be initiated (see *Neurosyphilis* on page 52).

Figure 12. Clinical presentations of secondary syphilis

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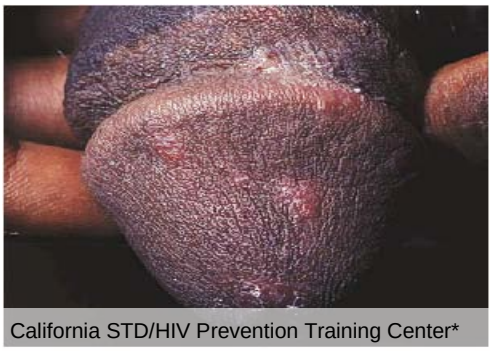
Macular rash.

California STD/HIV Prevention Training Center*

Macular and papulosquamous rash.

San Francisco City Clinic
Source: Dr. Joseph Engelman

Palmar rash.



California STD/HIV Prevention Training Center*

Papulosquamous rash (penis).

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Papulosquamous rash.

San Francisco City Clinic
Source: Dr. Joseph Engelman

Condyloma lata (anus).

California STD/HIV Prevention Training Center*

Mucous patches.

Centers for Disease Control and Prevention

Alopecia.

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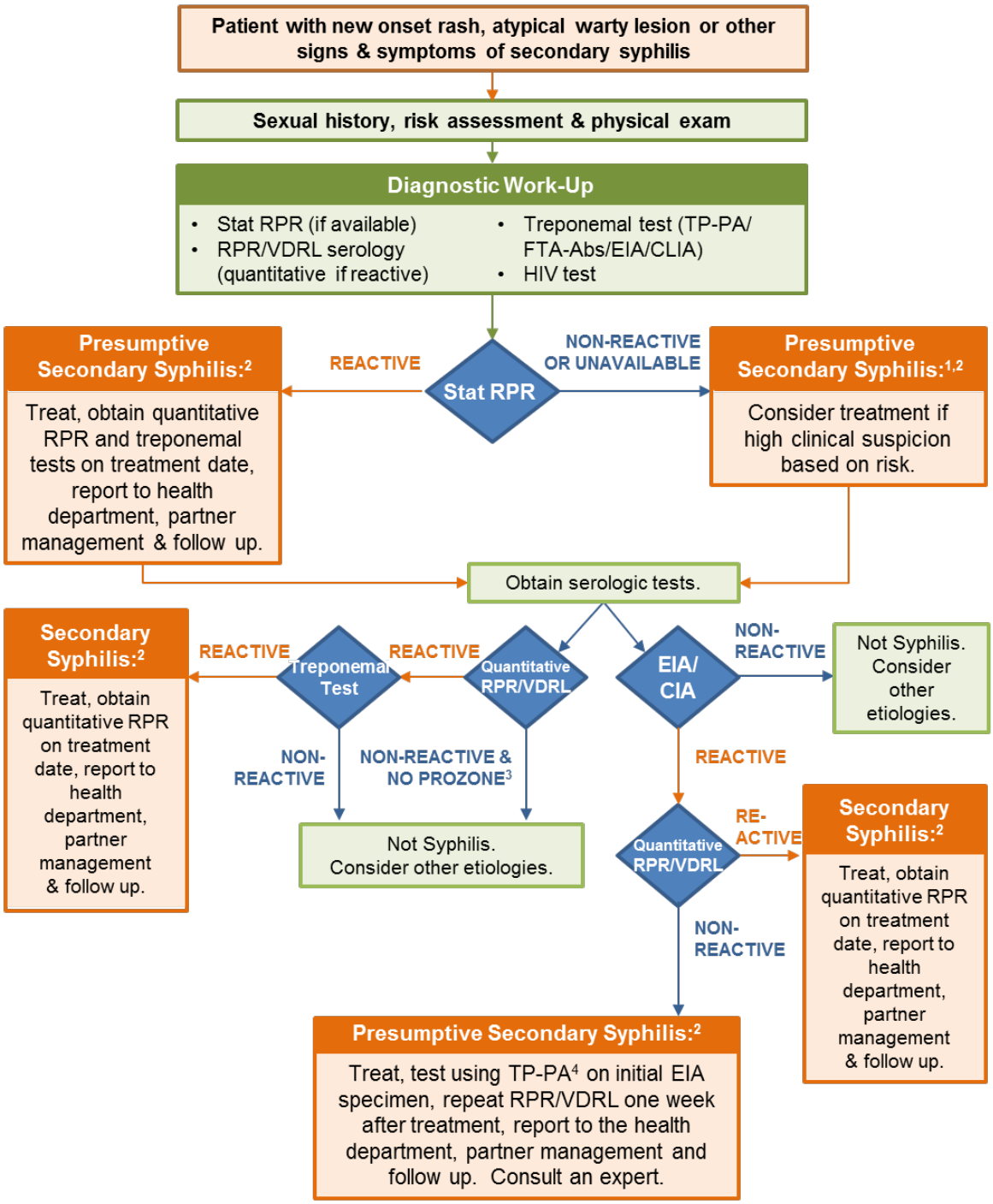
Figure 13. Algorithm for evaluating patients for secondary syphilis



Prepared by the California Department of Public Health

[1] If the patient is MSM or clinical exam with classic features secondary syphilis, consider presumptive treatment at the time of the initial visit before the diagnostic tests are available. Presumptive treatment is also recommended if patient follow-up is a concern.

[2] All patients with suspected syphilis should be tested for HIV infection and screened for other STDs. Repeat HIV testing of patients with secondary syphilis 3 months after the first HIV test, if the first test is negative.

[3] Prozone reaction is a false negative RPR or VDRL from excess antibody blocking the antigen-antibody reaction.

[4] FTA-Abs is no longer considered the gold standard treponemal test. TP-PA tests for a different antigen than EIA/CIA, and should be used for a second treponemal test when EIS/CIA is positive and RPR is non-reactive.

Latent Syphilis

Latent syphilis is asymptomatic and is identified through routine serologic screening.

Diagnostic Laboratory Testing

- Non-treponemal (RPR/VDRL) serologic testing is recommended, with reflex to treponemal (TP-PA/FTA-ABS/EIA/CIA) testing to confirm syphilis if reactive. Non-treponemal tests should be quantified for serologic follow-up, and to confirm current infection when treponemal tests are used for screening.[57]
- If treponemal immunoassays are used as the initial test (e.g. EIA or CIA), please consult the *Treponemal Test (EIA/CIA) Screening Algorithm* on page 17 for recommendations on interpretation of results. For more information regarding the use of treponemal immunoassays for syphilis diagnosis, consult the Reverse Sequence Syphilis Screening: Frequently Asked Questions.[58]

Staging

- Asymptomatic patients who acquired syphilis in the past 12 months are classified as having early latent syphilis. Early latent syphilis diagnosis is given if patient's only possible sexual exposure occurred in the past 12 months, or the patient has any of the following criteria in the past 12 months prior to evaluation:
    - Documented seroconversion of non-treponemal or treponemal tests or four-fold or greater increase in non-treponemal titer
    - Unequivocal symptoms of primary or secondary syphilis
    - Sex partner with documented primary, secondary or early latent syphilis
- Any patient who does not meet the above conditions should be classified as late latent syphilis or syphilis of unknown duration

Treatment

Early Latent (<1 year since last negative serology)

- Recommended Regimen
    - Benzathine penicillin G 2.4 million units IM in a single dose
- Alternative Regimens
    - Doxycycline 100 mg orally twice daily for 14 days, OR
    - Tetracycline 500 mg orally four times daily for 14 days, OR
    - Ceftriaxone 1 g IM or IV once daily for 10-14 days

Counsel patient about the possibility of a Jarisch-Herxheimer reaction, an acute febrile reaction frequently accompanied by headache, myalgias, fever, and other symptoms that usually occurs within the first 24 hours after the initiation of any therapy for syphilis. This reaction does not indicate allergy to antibiotic therapy. Over-the-counter nonsteroidal anti-inflammatory medications may be taken for symptomatic relief.

Late Latent Syphilis or Latent Syphilis of Unknown Duration

- Recommended Regimen
    - Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
- Alternative Regimens
    - Doxycycline 100 mg orally twice daily for 28 days, OR
    - Tetracycline 500 mg orally four times daily for 28 days

[57] Most patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity.
[58] www.cdph.ca.gov/programs/std/Documents/STD-301-Reverse-sequence-FAQs.pdf

Follow-Up

Follow-up Titers

HIV-negative patients should receive quantitative non-treponemal serologic tests at 6, 12, and 24 months for latent infection. HIV-infected patients should be evaluated clinically and serologically at 3, 6, 9, 12, and 24 months.

Successful Serologic Response

Serologic response to treatment is defined as a four-fold (or two-dilutional) decrease in the follow-up test titer in comparison to the titer obtained on the day of treatment (e.g., 1:128 to 1:32), over the 12 to 24 month period following treatment.

Serofast State

A persistent, low-level positive non-treponemal test titer (typically ≤1:8), reflecting a 'serofast' state, has been found to occur more frequently in HIV-infected patients with syphilis. In the absence of a sustained (greater than 2 weeks) 4-fold rise in titer and/or re-emergence of symptoms and signs following treatment, such persons should be followed at least annually with clinical evaluation, risk assessment, and repeat serology to assess the need for repeat treatment, and lumbar puncture should be performed if neurologic signs or symptoms emerge.

Treatment Failure

Treatment failure should be considered and a CSF examination should be performed if one of the following criteria is met:

1. Titers increase fourfold,
2. An initially high titer (≥1:32) fails to decline at least fourfold (i.e., two dilutions) within 12–24 months of therapy, OR
3. Signs or symptoms attributable to syphilis develop.

In such circumstances, even if the CSF examination is negative, retreatment for latent syphilis should be initiated.

Tertiary Syphilis

Background

Tertiary syphilis is very rare in the United States. Approximately one-third of people with untreated syphilis will develop late destructive lesions of syphilis many years following infection (3-20 years). These may be benign or may often affect the cardiovascular and/or central nervous system.

Diagnostic Laboratory Testing

- CSF examination for neurosyphilis should be conducted for suspected tertiary syphilis cases.

Treatment

In patients with *no evidence of neurosyphilis*, treatment is the same as late latent syphilis:

Recommended Regimens

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

Alternative Regimens

- Doxycycline 100 mg orally twice daily for 28 days, OR
- Tetracycline 500 mg orally four times daily for 28 days

Counsel patient about the possibility of a Jarisch-Herxheimer reaction, an acute febrile reaction frequently accompanied by headache, myalgias, fever, and other symptoms that usually occurs within the first 24 hours after the initiation of any therapy for syphilis. This reaction does not indicate allergy to antibiotic therapy. Over-the-counter nonsteroidal anti-inflammatory medications may be taken for symptomatic relief.

In patients with tertiary syphilis and neurosyphilis, treatment should be given for neurosyphilis (see *Neurosyphilis* on page 52).

Follow-Up

Limited information is available concerning clinical response and follow-up of patients who have tertiary syphilis. Consult an infectious disease expert for recommendations.

Neurosyphilis

Neurosyphilis can occur during any stage of syphilis. The CDC recommends a CSF examination only be performed if patients have clinical evidence of neurologic involvement, have suspected treatment failure, or are diagnosed with tertiary syphilis.

Symptoms

Clinical evidence of neurologic involvement can include cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and signs or symptoms of meningitis.

Diagnostic Laboratory Testing

The laboratory diagnosis of neurosyphilis usually depends on multiple laboratory abnormalities in the CSF. The following abnormalities may be present in an individual with neurosyphilis:

- CSF pleocytosis: >5 WBC/mm^3 in HIV-negative patients, >20 WBC/mm^3 in HIV-positive patients.
- Elevated CSF protein: range depends, consult local laboratory.
- Reactive CSF-VDRL: This is the standard serologic test for neurosyphilis. Unlike the serum VDRL, a reactive CSF-VDRL alone is sufficient to make a diagnosis of neurosyphilis. Sensitivity of the test varies – a patient with a non-reactive CSF-VDRL may still have neurosyphilis. Clinical correlation is recommended.

Non-reactive CSF FTA-ABS: although this test is not FDA approved for diagnostic use in the CSF, it may be used to *rule out* the diagnosis of neurosyphilis. Due to a high rate of false-positive results, it should not be used to make the diagnose neurosyphilis; however if the CSF-FTA-ABS is negative, neurosyphilis is highly unlikely.

Treatment

Recommended Regimens

- 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

Alternative Regimens

- Procaine penicillin G, 2.4 million units IM every four hours for 10-14 days, PLUS
- Probenecid 500 mg orally four times per day for 10-14 days

Follow-Up

If CSF pleocytosis was present initially, a CSF examination should be repeated every 6 months until the cell count is normal. Follow-up CSF examinations also can be used to evaluate changes in the CSF-VDRL or CSF protein after therapy; however, changes in these two parameters occur more slowly than cell counts, and persistent abnormalities might be less important. The leukocyte count is a sensitive measure of the effectiveness of therapy.[59]

If the cell count has not decreased after 6 months or if the CSF cell count or protein is not normal after 2 years, retreatment should be considered.

[59] STD Treatment Guidelines, 2015. MMWR. 2015;64(RR3). www.cdc.gov/std/tg2015/syphilis.htm