County of Los Angeles Public Health

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STD Clinic Manual

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Belongs to:

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COUNTY OF LOS ANGELES
Public Health

STD Clinic Manual

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STDs by Disease

Bacterial Vaginosis

Formerly called nonspecific vaginitis, Haemophilus vaginitis or Gardnerella vaginitis, bacterial vaginosis (BV) is the clinical result of alterations in the vaginal flora. It is not generally regarded as an STD except in women who have sex with women. It is a sexually related disease because it is more common in women with frequent exposure to semen. *Gardnerella vaginalis* (a small gram-negative pleomorphic coccobacillus), *Bacteroides sp.* (anaerobic gram-negative bacilli), *Mobiluncus sp.* (motile, anaerobic, curved gram-positive bacilli), prevotella and genital mycoplasmas and ureoplasmas have all been implicated. BV is manifested by a malodorous vaginal discharge that is often most noticeable after intercourse. Women with BV are at increased risk for the acquisition of some STDs (e.g., HIV, N. gonorrhoea,chlamydia and HSV- 2), complications after gynecologic surgery, complications of pregnancy, and recurrence of BV.

A. Diagnosis

1. History:
    a. Patients often complain of a fishy malodorous vaginal discharge (usually not itchy).
    b. Patients may be asymptomatic, but have all the signs of BV on exam.
    c. Many patients report recent and regular douching.
2. Examination:
    a. Classically, BV produces a homogeneous, thin, adherent, malodorous, white vaginal discharge.
    b. In the absence of other conditions, the remainder of the exam is normal.
3. Laboratory:
    a. Presence of clue cells on a saline preparation. Clue cells are epithelial cells with a granular appearance and over 70% of the edges obscured by adherent bacteria.
    b. Fishy odor noted immediately after KOH is added (positive whiff test).
    c. pH of vaginal discharge >4.5.
4. Diagnostic criteria (at least 3 must be present):
    a. Homogeneous thin gray or white, adherent discharge on the vaginal wall.
    b. pH of vaginal fluid higher than 4.5.
    c. A positive whiff test: fishy, amine odor from vaginal fluid, before or after mixing with 10% potassium hydroxide (KOH).
    d. Greater than 20% of epithelial cells are clue cells (or clue cell: epithelial cell ratio >1:5).

B. Treatment

Treatment is recommended for women with symptoms. The established benefits of therapy in non-pregnant women are to relieve vaginal symptoms and signs of infection.

Recommended regimen:

- **Metronidazole** 500 mg orally BID for 7 days

  or

- **Metronidazole** gel, 0.75%, one full applicator intravaginally QHS for 5 days **(more costly)**

C. Treatment of Persistent or Recurrent Bacterial Vaginosis

Data on effective treatment regimens for persistent or recurrent BV are limited. Women with persistent or recurrent symptomatic BV should be counseled regarding strategies to prevent BV (see F4 counseling points).

1. For persistent infection or the first recurrence, if compliance with medication was poor, retreat with the same regimen. If compliance was good, retreat with a different recommended regimen such as:
   - Clindamycin cream, 2%, one full applicator intravaginally QHS for 7 days (more costly and damages latex).
2. If multiple recurrences occur, the patient may be re-treated with a recommended regimen (oral metronidazole, metronidazole gel or clindamycin cream) or an alternative regime i.e.
   - **Clindamycin** 300 mg PO BID for 7 days

     or

   - **Tinidazole** 2g orally once daily for 2 days

     or

   - **Tinidazole** 1g orally once daily for 5 days

3. For patients with persistent recurrences (more than 3 episodes a year) consider suppressive therapy, although benefit might not persist when therapy is discontinued:

- Treatment with a recommended therapy followed by:
- Metronidazole gel 0.75% 5g (1 applicator) per vagina, QHS twice weekly for 4-6 months
- There is limited data on alternative suppressive therapies such as boric acid and metronidazole with fluconazole – see CDC Rx guidelines for further information.

D. Treatment in Pregnancy

1. BV has been associated with adverse pregnancy outcomes, although the mechanism remains poorly understood.
2. Treatment is recommended in symptomatic women.
3. The benefit of treatment of asymptomatic pregnant women, who have previously had a preterm delivery, has not been determined. It is best to leave the treatment of asymptomatic pregnant women with BV to the prenatal care provider.

Recommended Regimen:

- **Metronidazole** 500 mg po BID x 7 days

  or

- **Metronidazole** 250 mg po TID x 7 days

  or

- **Clindamycin** 300 mg orally BID x 7 days (more costly).

E. Follow-Up

1. Routine follow-up is not recommended for non-pregnant women.

F. Counseling/Patient Education

Patients should:

1. Understand how to take or use prescribed medications and be instructed to avoid alcohol 24 hours before and after metronidazole administration due to possible disulfiram-type reaction;
2. Return for evaluation if symptoms persist or recur after treatment;
3. Clindamycin products may weaken latex condoms and diaphragms, therefore cannot be relied upon during treatment and for 72 hours after treatment has been completed.
4. To avoid recurrence, patient should be advised to:
   - Abstain from vaginal sex during treatment.
   - Avoid douching
   - Clean sex toys (or use condoms) between use from one woman to another.
   - Avoid vaginal insertion following anal insertion of fingers or penises.
   - Use condoms during first month following treatment as this will probably reduce risk of recurrence.

G. Evaluation of Sex Partners

No clinical counterpart of BV is recognized in the male. The male partner can be offered a STD exam and appropriate screening and given relevant information on BV. However, treatment of male partners has not shown a reduction in BV recurrence in female partners.

Female partners of females diagnosed with BV have shown high rates of BV in several studies. Offer exam and evaluation of partner.

Candidiasis in Men

In men, the glans of the penis may become colonized with yeast. This condition is manifested by itchiness and red rash with white flat lesions on the glans, prepuce, coronal sulcus, and shaft. Uncircumcised men tend to have more symptoms. If inflammation continues, men may exhibit shallow ulcerations on the glans. As in women, this condition is generally not sexually transmitted and partner referral is not necessary. After unprotected intercourse with a woman who has *Candida* vaginitis, a man may experience transient erythema and burning of the glans. This may occur as early as minutes after intercourse, is alleviated by washing, and occurs more frequently in uncircumcised men.

A. Diagnosis

1. History:
    a. Rash on glans and/or prepuce.
    b. May be itchy.
    c. Candidiasis in sexual partners.
    d. Diabetes mellitus.
2. Examination:
    a. Red rash with white flat lesions and possibly shallow ulcerations on glans, prepuce, and shaft.
    b. Excoriations may be present.
3. Laboratory:
    a. A KOH preparation of a skin scraping may reveal pseudohyphae or budding yeast.
4. Diagnostic criteria:
    a. History and clinical appearance consistent with balanitis.

B. Treatment

Any of the following topical OTC antifungal preparations are effective. Note that these preparations may damage latex condoms and diaphragms.

- Clotrimazole 1% cream BID x 7-14 days
- Miconazole 2% cream BID x 7-14 days (not on PH formulary, available OTC)
- Tolnaftate 1% (Tinactin) cream BID x 7-14 days

All are available without prescription. Area under the prepuce should be kept clean and dry. Creams should be applied in a thin layer twice a day until balanitis has resolved. Most cases should resolve within one to two weeks. Keeping the affected area dry is important.

Severe candidiasis may be treated with one dose of fluconazole 150 mg po stat.

C. Follow-up

Routine follow up is not required.

D. Special considerations

Predisposing factors such as HIV infection and diabetes should be considered. Patients who may be at risk for HIV infection should be counseled regarding HIV antibody testing. Patients with symptoms of diabetes, a family history of diabetes or recurrent *Candida* balanitis should have a urine dipstick test to screen for glucosuria. If glucosuria is present, patients need referral to a primary care provider.

Candidiasis in Women

Vulvovaginal candidiasis (VVC) is not considered to be sexually transmitted. Most infections are caused by the dimorphic fungus *Candida albicans* which is microscopically visible as oval buds and/or pseudohyphae. This common disorder is manifested by vulval and/or vaginal itching, redness, or a discharge. Women who are immunosuppressed, diabetic, or pregnant are at greater risk for Candida vaginitis. Many women are asymptomatically colonized with *C. albicans.*

A. Diagnosis

1. History:
    a. Patients may complain of vaginal discharge and/or vaginal/vulvar itching or burning and/or external dysuria (vulval pain on micturition) and dyspareunia.
    b. Note recent use of oral contraceptives, topical or systemic steroids, symptoms or diagnosis of diabetes, HIV infection or other risk factors for immunosuppression.
2. Examination:
    a. White, thick, cheesy vaginal discharge. Occasionally, discharge is scant.
    b. Vulva may be red, swollen, and may have excoriations or very shallow ulcerations or fissures.
3. Laboratory:
    a. Budding yeast and/or pseudohyphae on a saline or KOH preparation. The wet mount has low sensitivity, approximately 50%.
4. Diagnostic criteria:
    a. Typical clinical findings, yeast (budding cells) or pseudohyphae on microscopic examination of a smear of vaginal discharge by Gram's stain, potassium hydroxide wet mount preparation (10% KOH), or saline wet mount. The pH will be in the normal range of 4.0 to 4.5. Remember that mixed infection can occur.

B. Treatment

About 10-20% of women are colonized with yeast organisms without symptoms. Treatment is only indicated if symptoms are present. For symptomatic women with negative wet mounts, empiric treatment can be considered if there is any sign of VVC on examination,. Any of the following antifungal preparations are effective.

Intravaginal Agents:

If vulvitis is present, a cream prepration is preferred so the patient can apply to the vulva in addition to intravaginally. Note that some of these products may damage latex condoms and diaphragms.

Clotrimazole 1% cream 5 g intravaginally for 7–14 days (also available OTC)
or
Terconazole 0.8% cream 5 g intravaginally for 3 days
or
Terconazole 80 mg vaginal suppository, one suppository for 3 days

The preparations below, which are not on the Public Health Formulary, are also effective and available OTC.

Butoconazole 2% cream 5 g intravaginally for 3 days
or
Clotrimazole 2% cream 5 g intravaginally for 3 days
or
Miconazole 2% cream 5 g intravaginally for 7 days
or
Miconazole 4% cream 5 g intravaginally for 3 days
or
Miconazole 100 mg vaginal suppository, one suppository for 7 days
or
Miconazole 200 mg vaginal suppository, one suppository for 3 days
or
Miconazole 1,200 mg vaginal suppository, one suppository for 1 day
or
Tioconazole 6.5% ointment 5 g intravaginally in a single application

Other intravaginal medications are available by prescription but are not on the DPH formulary (see CDC guidelines for details).

Oral Agent:

Fluconazole 150 mg oral tablet, one tablet in a single dose

Note: Clinically important drug interactions can occur with oral azoles. Fluconazole should not be used in pregnancy.

C. Treatment in Pregnancy

In pregnancy, only topical imidazoles are recommended, using the 7 day regimes described for non-pregnant women. Suppositories are preferred to cream as they can be inserted digitally without the use of applicators. **Fluconazole should not be used.**

D. Follow-up

Patients with frequent or chronic candidal vulvovaginitis may be more difficult to treat; they should be evaluated for predisposing conditions (especially HIV infection and diabetes).

E. Counseling/Patient Education

Patients should:

1. Understand how to take or use medications;
2. Return for evaluation if symptoms persist or recur after treatment; and
3. Understand that many yeast creams are oil-based and may break down latex condoms and diaphragms.

F. Evaluation of Sex Partners

Treatment of sex partners is usually not necessary unless the partner has candida balanitis.

G. Recurrent Candidiasis

Recurrent vulvo vaginal candidiasis (RVVC), usually defined as four or more episodes of symptomatic VVC in 1 year, affects a small percentage of women (<5%). The pathogenesis of RVVC is poorly understood, and the majority of women with RVVC have no apparent predisposing or underlying conditions. HIV, pregnancy and diabetes should be excluded. Refer patient to primary provider for vaginal culture and treatment (for further information see CDC guidelines).

H. Severe Vulvo Vaginal Candiasis

Severe vulvovaginitis (i.e., extensive vulvar erythema, edema, excoriation, and fissure formation) is associated with lower clinical response rates in patients treated with short courses of topical or oral therapy. Either 7–14 days of topical azole or 150 mg of fluconazole in two sequential doses (second dose 72 hours after initial dose) is recommended.

Chancroid

Chancroid is a sexually transmitted infection caused by *Haemophilus ducreyi*, a gram-negative bacterium. It is characterized by painful, non-indurated genital ulcerations with irregular, undermined borders. Unilateral or bilateral tender adenopathy occurs in approximately half the patients and an inguinal bubo (swollen abcess) may occur. *H. ducreyi* has a short incubation period (on average 4-7 days, with a range of 3-10 days) which may help distinguish it from other causes of genital ulcer disease. There is never a vesicular stage but chancroid may present initially as a small pustule that may be mistaken for folliculitis. It may also present as a raised, beefy red lesion. Complications of chancroid include phimosis or paraphimosis and ruptured buboes, which may result in fistulae. It occurs in Africa, Central and South America, the Caribbean, Asia and South East U.S.A.

Chancroid is a cofactor for HIV transmission; high rates of HIV infection among patients who have chancroid occur in the United States and other countries. Approximately 10% of persons who have chancroid that was acquired in the United States are coinfected with *T. pallidum* or HSV; this percentage is higher in persons who have acquired chancroid outside the United States.

A. Diagnosis

1. History:
    a. Male patients may present with a painful genital ulcer(s) and inguinal swelling or pain; female patients may present with a vulvar or vaginal ulcer(s) or with dysuria, bleeding, or vaginal discharge. Ulcer(s) in women may be relatively painless.
    b. Obtain the following important historical characteristics:
        - Duration of ulcer(s).
        - Associated pain.
        - Last sexual contact (may help to identify etiologic agent by an obvious incubation period) and if there was sex worker contact. Note any travel history and sex contacts in areas outside LA County (South East U.S., Africa, Central or South America, Caribbean, and Asia).
        - Use of systemic or topical antimicrobial agents or other topical preparations (steroids, etc,).
        - Signs or symptoms in partner(s).
        - Past history of ulcers and similarity of previous ulcers to current ulcer(s).
        - Review history of previous STDs. If patient has a history of syphilis, obtain treatment history, date and titer of the last RPR.
        - HIV status, if known by patient.

2. Examination:
    a. There may be a single ulcer or multiple ulcers, frequently in a linear pattern.
    b. The ulcer typically begins as a pustule and then erodes within a few days. It has undermined edges that can be ragged or serpiginous in appearance. Rectangular shaped ulcers are considered characteristic. The ulcers are usually sharply demarcated, but they may become confluent and quite large. They are generally not indurated, and are usually friable and deep. The base may be covered by a grey or yellow necrotic purulent exudate. Tenderness is usually, although not always, present. Painful and tender inguinal adenopathy is present in approximately 50% of patients.

        A bubo is an enlarged inguinal lymph node that is tender and fluctuant. The skin overlying a bubo is often erythematous, quite thin and tense.
    c. Note the following characteristics:
        - Number of ulcers.
        - Location.
        - Shape (oval, round, serpiginous, rectangular).
        - Size.
        - Nature of the ulcer(s) edges (raised, flat, undermined).
        - Base of ulcer (purulent, clean).
        - Depth of largest ulcer.
        - Tenderness.
        - Induration.
        - Friability.
        - Circumcision status of male.
        - Inguinal adenopathy/bubo.

3. Laboratory:
    a. Obtain Aimes transport media/swab package, verifying that media is within expiration date. Cleanse the ulcer with sterile non-bacteriostatic saline to expose the base. Moisten applicator swab with sterile non-bacteriostatic saline and collect exudate from the edge and base of the lesion.
    b. Place applicator swab in transport media tube and replace cap firmly to completely seal. Keep refrigerated at 2 - 8° C until transported to laboratory on an ice pack. Specimen must be received at the Bacteriology section within 48 hours of the specimen being collected from the patient.
    c. Order test with MISYS or standard laboratory test requisition form (check box for "Other" and write in "Chancroid exam")

       MISYS test code "ABCR"
       - SDES: LESW (code translation – Lesion swab)
       - SREQ:-;Chancroid

4. Diagnostic criteria:
    a. Clinical criteria, which will always be the necessary first step in diagnosis, is based on the presence of painful ulcers on the genitalia (atypical ulcers may be painless), possibly accompanied by enlarged and tender inguinal nodes. The laboratory criteria involve isolation and confirmed identification of *H. ducreyi* on enriched medium from a genital ulcer. Cultures take 3-5 days for confirmation. Sensitivity of culture less than 80%.

       A probable diagnosis of chancroid, for both clinical and surveillance purposes, can be made if all of the following criteria are met:

       - The patient has one or more painful genital ulcers.
       - The clinical presentation, appearance of genital ulcers and, if present, regional lymphadenopathy are typical for chancroid.
       - The patient has no evidence of *T. pallidum* infection by a serologic test for syphilis performed at least 7 days after onset of ulcers.
       - A test for HSV performed on the ulcer exudate is negative.

B. Treatment

1. Medication

- **Ceftriaxone** 250 mg IM in a single dose

  or

- **Azithromycin** 1 gram PO in a single dose

  Or

- **Ciprofloxacin*** 500 mg PO BID for 3 days

  or

- **Erythromycin** base 500 mg TID for 7 days.

Azithromycin and ceftriaxone offer the advantage of single-dose therapy.

Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported.

Successful treatment for chancroid cures the infection, resolves the clinical symptoms, and prevents transmission to others. In advanced cases, scarring can result, despite successful therapy.

2. **Pregnant and lactating women**

Ciprofloxacin is contraindicated for pregnant and lactating women.

3. **HIV Infected patients**

HIV-infected patients who have chancroid should be monitored closely because, as a group, these patients are more likely to experience treatment failure and to have ulcers that heal more slowly. HIV-infected patients might require longer courses of therapy than those recommended for HIV-negative patients, and treatment failures can occur with any regimen. Because evidence is limited concerning the therapeutic efficacy of the recommended ceftriaxone and azithromycin regimens in HIV-infected patients, these regimens should be used for such patients only if follow-up can be ensured. Some specialists prefer the erythromycin 7-day regimen for treating HIV-infected persons.

4. **Management of Buboes**

Clinical resolution of fluctuant lymphadenopathy is slower than resolution for ulcers and might require needle aspiration or incision and drainage to prevent rupture and subsequent fistula formation. Although needle aspiration of chancroid buboes is a simple procedure, incision and drainage might be preferred because of a reduced need for repeat drainage procedures. Patients should be referred for aspiration or incision and drainage. A bubo may continue to enlarge even after successful therapy of the ulcer, so careful follow-up of a bubo is necessary.

C. Follow-up

1. Patients with presumed or confirmed chancroid should be re-examined 3-7 days after beginning therapy. If treatment is successful, ulcers usually improve symptomatically within 3 days i.e. ulcers less painful and the patient should be feeling better. Partial healing should be evident seven days after therapy begins. The patient should return at weekly intervals until complete healing occurs.
2. If no clinical improvement is evident, the clinician must consider whether 1) the diagnosis is correct, 2) the patient is coinfected with another STD, 3) the patient is infected with HIV, 4) the treatment was not used as instructed, or 5) the *H. ducreyi* strain causing the infection is resistant to the prescribed antimicrobial.
3. The time required for complete healing depends on the size of the ulcer; large ulcers might require >2 weeks. In addition, healing is slower for some uncircumcised men who have ulcers under the foreskin. Clinical resolution of fluctuant lymphadenopathy is slower than resolution for ulcers.
4. Since more than one organism may co-exist in a genital ulcer and the incubation period for chancroid is shorter than that of syphilis and HIV, patients should have an RPR repeated one week and six weeks after therapy. HIV antibody testing should be encouraged in any patient with negative or unknown HIV serostatus at the time of first visit and three months later.

D. Counseling/Education

Patients should:

1. Be referred for PHI interview and counseling;
2. Understand how to take prescribed oral medications;
3. Avoid sex for at least 7 days and until the patient and partner(s) have completed therapy;
4. Use condoms to prevent future infections; and
5. Understand that chancroid has been associated with an increased risk of acquiring and transmitting HIV infection.

E. Evaluation of Sex Partners

1. All sex partners of patients who have *H. ducreyi* infection should be examined and promptly treated with an appropriate regimen for *H. ducreyi* if the exposure took place within 30 days before the onset of symptoms of the infected patient. Partners should be treated even with negative exams.

F. Reporting

1. Send CMR to STD Program within 7 days of diagnosis.

Chlamydia Trachomatis

Infection caused by *Chlamydia trachomatis* is one of the most prevalent STDs in the United States. The single most important risk factor is young age. History of multiple partners, other STDs, and past infection with chlamydia are other risk factors. Infections in both women and men commonly occur without symptoms or signs. Women may complain of urinary frequency and dysuria; an increase in vaginal discharge; or lower abdominal pain. Men may have symptoms that may include urethral itch, dysuria, and a mucoid-to-purulent discharge. Serious complications related to chlamydia infection include epididymitis in men; endometritis, salpingitis, infertility, ectopic pregnancy, and postpartum infection in women; and conjunctivitis and pneumonia in infants. Chlamydia infection can also trigger Reiter's syndrome, the triad of urethritis, arthritis and conjunctivitis, with or without other cutaneous or mucous membrane lesions such as, keratoderma blemorrhagica, circinate balanitis/vulvitis, uveitis, oral ulceration, cardiac or neurological involvement. Chlamydia trachomatis has a variable incubation period of approximately 7-21 days, but may be up to several months. Lymphogranuloma venereum (LGV), a rare disease caused by other serovars of *C. trachomatis is* discussed in a separate section.

A. Diagnosis

1. History:
    a. Male patients may complain of dysuria and/or urethral discharge; typically the symptoms tend to be milder than for gonococcal urethritis and the majority of men are asymptomatic. Rectal chlamydial infections may be asymptomatic, or may resemble gonococcal proctitis with pain, bleeding and mucous discharge.
    b. Female patients may have no symptoms. If symptomatic, women may complain of vaginal discharge, urinary frequency and dysuria, lower abdominal pain, intermenstrual bleeding and dsyparuenia.
    c. For symptoms of complicated infections in men and women, refer to the epididymitis and PID protocols.

2. Examination:
    a. Male patients with a urethral chlamydial infection may have a mucoid or purulent urethral discharge usually without inguinal adenopathy, although the exam may be normal.
    b. Female patients may have signs of cervicitis, although the exam may be normal.
    c. Male and female patients reporting receptive anal sex may have signs of proctitis, although the exam may be normal.

3. Laboratory:
    a. Nucleic acid amplification testing (NAAT) should be used to diagnose chlamydia in the cervix, urethra and rectum. The best genital tests in women are cervical or self collected vaginal swabs (SCVS). Urine specimens should only be used for women who are not having a pelvic examination and who refuse to collect a SCVS. Urine NAAT testing is performed on a first void urine (i.e. the first 10-15cc of urine specimen collected), preferably more than two hours after the patient last urinated.
    b. Chlamydia Testing / screening guidelines - See table.
        - Diagnostic testing at exposed sites should be performed for all individuals with symptoms or syndromes potentially caused by Chlamydia.
        - Contacts to chlamydia need to be tested based on site exposed, and treated epidemiologically.
        - If medicolegal case, culture all sites exposed.

4. Diagnostic criteria:
    a. Positive test by NAAT of urine, vaginal, cervical, rectal, or urethral specimen.
    b. A positive Chlamydia culture.
    c. Detection of *C. trachomatis* by a non-culture method (Chlamydiazyme or other method) from the cervix or urethra.
    d. Re-testing is not indicated for patients attending the clinic with documented *C. trachomatis* (by provider letter or laboratory form).

LAC STD Clinics - Gonorrhea & Chlamydia Screening / Testing

	Site of Exposure / *Test used*		
	Genital *GC/CT* *Self-collected Vaginal Swab, Urine or Cervix (F) Urine or Urethra (M)*	**Rectum** *GC/CT*	**Pharynx** *GC*
MSM	▪ Each new visit	▪ Test if rectal symptoms present *-or-* ▪ Screen at least annually, if practices receptive anal sex	▪ Test if pharyngeal symptoms present *-or-* ▪ Screen at least annually, if practices receptive oral sex (mouth on partner's penis)
MSW	▪ Each new visit	▪ Not applicable	▪ Test if pharyngeal symptoms present* *-or-* ▪ Screen if contact has GC
Women**	▪ Each new visit	▪ Test if rectal symptoms present *-or-* ▪ Screen if H/O anal receptive sex in last 90 days	▪ Test if pharyngeal symptoms present* *-or-* ▪ Screen if contact has GC *-or-* ▪ Screen if patient reports sex for money/drugs

MSM - Men who have sex with men MSW - Men who have sex with women

- **<u>Only test /screen the site if it has been exposed</u>** UNLESS you suspect disseminated gonorrhea infection (DGI). If you suspect DGI, all sites should be tested for gonorrhea regardless of exposure.
- *Test if pharyngeal symptoms present and upper respiratory tract infection not suspected
- **Women - There is little data regarding prevalence of CT/GC among women who have sex exclusively with women, however, if symptomatic and site exposed, testing may be indicated.
- If patient has GC &/or CT, tests should be repeated 3 months after treatment.

B. Treatment

Recommended Regimens:

- Azithromycin 1 gram PO in a single dose

  OR

- Doxycycline 100 mg PO BID for seven days

Alternative Regimens:

- Erythromycin base 500mg PO QID x 7 days

  OR

- Erythromycin ethylsuccinate 800mg PO QID x 7 days

  OR

- Levofloxacin 500 mg PO QID x 7 days

  OR

- Ofloxacin 300 mg PO BID for 7 days (not on PH formulary)

Treatment in Pregnancy

A test of cure three-four weeks after completion of any treatment regimen is recommended in pregnancy.

Recommended Regimens:

- Azithromycin 1 gram PO in a single dose

  OR

- Amoxicillin 500 mg PO TID for 7 days

Alternative Regimens in Pregnancy:

- Erythromycin base 500 mg PO QID x 7 days

  OR

- Erythromycin base 250 mg PO QID x 14 days

  OR

- Erythromycin ethylsuccinate 800 mg PO QID x 7 days

  OR

- Erythromycin ethylsuccinate 400 mg PO QID x 14 days

C. Follow-up

Taken as directed, the recommended antimicrobials are highly effective and post-treatment tests are not necessary for compliant patients (unless pregnant). Note that for 3 weeks after completion of therapy, any non-culture test, such as NAAT may yield false-positive results. If there is strong suspicion of non-compliance or of re-infection, empiric treatment should be given.

All infected men and women should have repeat testing 3 months after completing treatment to rule out re-infection (see 'Re-Testing Chlamydia and/or Gonorrhea Positive Men & Women Three Months after Treatment' protocol).

D. Counseling/Education

Patients should:

1. Be counseled that Chlamydia is an STD and about sequelae.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Discuss management of all sex partner(s) within 60 days of onset of symptoms or diagnosis or the most recent partner, if last sexual contact was more than 60 days ago (see section E).
5. Avoid sex for at least 7 days after patient and all current sex partner(s) have completed therapy.
6. Use condoms to prevent future infections.
7. **Return in 3 months for repeat testing** (see 'Re-Testing Chlamydia and/or Gonorrhea Positive Men & Women Three Months after Treatment' protocol).

E. Management of Sex Partners

1. Treat all sex partner(s) within 60 days of onset of symptoms or diagnosis or the most recent partner (if last sexual contact was more than 60 days ago).

2. The first-choice strategy for managing partners of patients with chlamydia is to attempt to have all sex partners evaluated, tested, and treated for chlamydia and other STDs by a provider.

3. Patient-delivered partner therapy (PDPT) is an alternative partner management strategy for partners of patients with chlamydia whose prompt treatment cannot otherwise be ensured. As PDPT is equal to or better than traditional partner management strategies (self-referral or PHI notification), this method should be seriously considered. (See PDPT protocol)

F. Reporting

Send CMR to STD Program within 7 days of diagnosis.

Appendices (on STD Program intranet page)

- California Guidelines for Chlamydia and Gonorrhea Field Delivered Therapy
- Re-Testing Chlamydia and/or Gonorrhea Positive Men & Women after 3 Months after Treatment
- Patient Delivered Partner Therapy (PDPT)
- Gonorrhea & Chlamydia Screening / Testing Guidelines
- Chlamydia and Gonorrhea Testing using Self Collected Vaginal Swabs: STDP Recommendations
- Instructions for self-collected vaginal swabs - English and Spanish

Gonorrhea

Infections caused by *N. gonorrhoeae* (GC) may be symptomatic or asymptomatic. GC can infect the urethra, cervix, rectum, pharynx, and in rare cases, may become disseminated (blood borne). It has a short incubation period of 1-10 days (average 2-5). Infections caused by antimicrobial-resistant *N. gonorrhoeae* are clinically indistinguishable from those caused by antimicrobial-susceptible strains.

Symptomatic men usually have purulent urethral discharge often accompanied by pain with urination. Women may have abnormal vaginal discharge, abnormal menses, pelvic pain, or pain with urination. Although the data on asymptomatic infection are limited, as many as 50-70% of women may have asymptomatic urethral/cervical infections and less than 10% of men have asymptomatic urethral infection. The majority of gonococcal infections in the rectum and pharynx are asymptomatic.

Serious complications of gonococcal infection include pelvic inflammatory disease with subsequent infertility and ectopic pregnancy in women, and epididymitis and urethral stricture in men. Disseminated gonococcal infection (DGI) may occur in either gender**,** but is not common. Untreated infection in pregnancy may result in premature delivery (including stillbirth). Newborns of women with untreated infection are at risk for *ophthalmia neonatorum*, scalp abscess at the site of fetal monitors, and disseminated infections.

Gonorrhea treatment is complicated by the ability of N. gonorrheoeae to develop resistance to antibiotics. Quinolone-resistant N. strains are widely disseminated throughout the US and so flouroquinolones should not be used to treat GC and associated conditions, such as PID. Cephalosporins are the only remaining class of antimicrobials recommended to treat GC. As there is evidence of decreasing N. gonorrheoeae susceptibility to cephalosporins, particularly oral regimens, DPH clinicians should be on the lookout for potential treatment failures.

A. Diagnosis

1. History: Symptoms, when they occur, vary depending on the site of infection.
    a. Women may present with vaginal discharge, lower abdominal pain, pain with intercourse, dysuria, post-coital and intermenstrual bleeding.
    b. Men usually present with pain with urination or discharge.
    c. Rectal infection in men and women may present as proctitis - discharge (usually described as mucous on stools), tenesmus, perianal itching, rectal pain and possibly rectal bleeding.
    d. Pharyngeal infection in men and women, though usually asymptomatic may present with sore throat or pain with swallowing
    e. DGI –see section G.

2. **Examination:** Signs of infection may or may not be present.

   a. Cervix – mucopurulent or frankly purulent cervical discharge, redness, and friablity.

   b. Urethra – purulent discharge, possibly phimosis and swelling, tender inguinal adenopathy.

   c. Rectum – purulent exudate (clinicians must use anoscope for proper rectal examination).

   d. Pharynx – redness, exudute (most have no signs of infection and when present are nonspecific).

3. **Laboratory:**

   a. Nucleic acid amplification testing (NAAT) should be used to diagnose gonorrhea in the cervix, urethra, oropharynx and rectum. The best genital tests in women are cervical or self collected vaginal swabs (SCVS). Urine specimens should only be used for women who are not having a pelvic examination and who refuse to collect a SCVS. Urine is the preferred specimen for men practicing insertive sex. Urine NAAT testing is performed on a first void urine (i.e. the first 10-15cc of urine specimens collected), preferably more than two hours after the patient last urinated.

   b. For medicolegal cases in adults, NAATs are the preferred diagnostic test due to high sensitivity and specificity. In children, culture should be performed in addition to NAAT.

   c. For suspected treatment failures, culture should be performed (see section D. follow-up). Without an incubator culture specimens need to be transported to the PHL within 1-2 hours of inoculation.

   d. See laboratory section on Gonorrhea, ‘How to perform and request gonorrhea cultures’ (appendix 1):

      - How to obtain and maintain the modified Thayer Martin medium culture plates from PHL
      - How to collect, inoculate and maintain culture specimens
      - How to order GC culture on MYSIS
      - List of STD clinics with incubators.

4. Diagnostic Criteria:

a. Isolation of *N. gonorrhoeae* from sites of exposure (e.g. vagina, urethra, pharynx, endocervix, rectum) by culture or positive NAAT.

b. Testing / screening guidelines - See table

LAC STD Clinics - Gonorrhea & Chlamydia Screening / Testing

	Site of Exposure / *Test used*		
	Genital *GC/CT* *Self-collected Vaginal Swab, Urine or Cervix (F) Urine or Urethra (M)*	**Rectum** *GC/CT*	**Pharynx** *GC*
MSM	▪ Each new visit	▪ Test if rectal symptoms present *-or-* ▪ Screen if H/O anal receptive sex in last 90 days, or at least annually.	▪ Test if pharyngeal symptoms present *-or-* ▪ Screen if H/O pharyngeal receptive sex in last 90 days, or at least annually.
MSW	▪ Each new visit	▪ Not applicable	▪ Test if pharyngeal symptoms present* *-or-* ▪ Screen if contact has GC
Women**	▪ Each new visit	▪ Test if rectal symptoms present *-or-* ▪ Screen if H/O anal receptive sex in last 90 days	▪ Test if pharyngeal symptoms present* *-or-* ▪ Screen if contact has GC *-or-* ▪ Screen if patient reports sex for money/drugs ▪ Screen if other high risk exposure

MSM - Men who have sex with men MSW - Men who have sex with women

- **<u>Only test /screen the site if it has been exposed</u>** UNLESS you suspect disseminated gonorrhea infection (DGI). If you suspect DGI, all sites should be tested for gonorrhea regardless of exposure.
- *Test if pharyngeal symptoms present and upper respiratory tract infection not suspected
- **Women - There is little data regarding prevalence of CT/GC among women who have sex exclusively with women, however, if symptomatic and site exposed, testing may be indicated.
- If patient has GC &/or CT, tests should be repeated 3 months after treatment.

B. Treatment

Uncomplicated gonococcal Infections of the cervix, urethra, rectum and pharynx

Recommended regimen:
Ceftriaxone 250 mg intramuscularly in a single dose
PLUS
Azithromycin 1 g orally single dose *OR* Doxycycline 100 mg orally BID for 7 days

Alternative regimen*:
Cefixime 400 mg orally in a single dose
PLUS
Azithromycin 1 g orally single dose *OR* Doxycycline 100 mg orally BID for 7 days

*Note: Test of cure should be performed if pharyngeal infection treated with alternative regimen. Doxycyline should not be used in pregnant or lactating women.

IgE-mediated (hives or history of anaphylaxis) allergies to penicillin, where the use of cephalosporins is a concern, or patients with allergies to cephalosporins:
Azithromycin 2 g orally in a single dose with test-of-cure (TOC)

C. Follow-up

1. Retest in 3 months
   All men and women with confirmed gonorrhea should be re-tested 3 months after treatment (see protocol for 'Re-Testing Chlamydia and/or Gonorrhea Positive Men & Women Three Months after Treatment).
2. Test-of-cure (TOC)

   Indications

   TOC is indicated when less effective treatment regimens are used or in pregnant women. Examples of this would be, pharyngeal infections treated with oral medication and any GC treated with azithromycin only.

   Method of TOC

   The preferred method of TOC is gonorrhea culture 1 week post treatment. Clinics should try to obtain culture plates in time for patient return visit or refer patient to a clinic with culture capability. If this is not possible, then repeat nucleic acid amplification testing (NAAT) 3-4 weeks after treatment should be performed.

3. Treatment failure

Patients presenting with persistent symptoms in the absence of re-exposure or those with a positive test of cure should be considered potential treatment failures. Patients should be questioned regarding the possibility of re-infection, including any new sex partners or repeated exposure to an untreated partner.

If treatment failure is suspected do the following:

a. Take a specimen for GC culture and antibiotic susceptibility testing from each site with symptoms or a positive NAAT TOC. . See Appendix 1 'How to take GC cultures'. On Sunquest, enter the code for treatment failure (TRFA) at the SREQ prompt.

b. Retreat patient with at least 250 mg of cetriaxone IM plus azithromycin or doxycycline.

c. Request that PHI prioritize the case for partner elicitation and notification.

d. Report to STDP by calling 213 744 3070 and ask to speak to the clinician on call.

D. Counseling/Education

Patients should:

1. Be educated regarding the importance to have all sex partners treated.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Avoid sex for 7 days, and
5. Use condoms to prevent future infections.

E. Evaluation of Sex Partners

All sex partners of the following patients who have *N. gonorrhoeae* infection should be examined, tested, and promptly treated for *N. gonorrhoeae* and *C. trachomatis* according to the following:

1. Partners should be treated if the exposure took place within 60 days before the onset of symptoms of the infected patient, or initial diagnostic test of the patient. If no partners in last 60 days, treat the last partner.

2. Partner-delivered therapy should be considered as a treatment option option for heterosexual men and women's partners (effective Jan 1, 2007) whose prompt treatment cannot be ensured or is unlikely. Men should be strongly encouraged to refer female partners to the clinic or MD for evaluation. See CHS Policy 314 Patient Delivered Partner Therapy for Chlamydia and Gonorrhea.

F. Reporting

Send CMR to STD Program within 7 days of diagnosis.

G. Disseminated Gonococcal Infections (DGI)

Although the incidence of DGI has declined, it is important to note *N. gonorrhoeae* can cause bacteremia and systemic infection including arthritis, meningitis, endocarditis, tenosynovitis and diffuse skin eruption characterized by small pustules. DGI should be considered if a patient has signs of toxicity, fever, pustular skin lesions, stiff neck, headache, acute swelling, pain, erythema of a joint (often a single joint) and/or tenosynovitis - redness, swollen or tender tendon sheath(s). Test all sites (genital, oral, rectal) for gonorrhea and refer to hospital for blood culture and other work up.

Hospitalize for initial therapy, especially for patients who cannot comply with recommended treatment, those in whom the diagnosis is uncertain, or those with purulent synovial effusions or other complications. Observe closely for endocarditis or meningitis. Treat presumptively for *C. trachomat*is.

Recommended therapy for DGI

Parenteral therapy should be provided for 24-48 hours after clinical improvement begins, at which time therapy can be switched to oral therapy to complete at least one week of therapy.

Parenteral therapy

Recommended regimen:

Ceftriaxone 1 gm IM or IV every 24 hours, followed by oral therapy

Alternative regimen*:

Cefotaxime 1g IV every 8 hours, followed by oral therapy
Ceftozoxime 1g IV every 8 hours, followed by oral therapy

Followed-by oral therapy

Cefixime 400 mg orally BID to complete at least one week of total antimicrobial therapy.

GONORRHEA CULTURE INSTRUCTIONS

Ordering supplies

Swabs
Order the following swabs on the online requisition system (OLR).

Swabs for urethral cultures (mini-swabs)
Puritan 25-800-A-50 swabs (Box of 50)
Calcium Alginate Tipped Sterile Applicators/Swabs with Aluminum Shaft
0.035" Diameter x 5-1/2" Length

Swabs for rectal, throat and cervical cultures
Puritan 25-806-1PD swabs (Box of 100)
Polyester (Dacron) Tipped Sterile Applicators/Swabs with Semiflexible Shaft
1/10" Diameter x 6" Length

Gono-Paks
Order Modified Thayer Martin (MTM) media and CO2 pills by requesting "GC - pill pocket plates" on the laboratory supply request form and faxing to the Public Health Laboratory's Containers/Support Services Section, phone (562) 658-1446, fax (562) 401-5985. State the number of plates required (they come in sleeves of 10 but individual plates can be ordered).

Storing supplies

Store plates sealed in plastic sleeves in the refrigerator (2-8°C) in an inverted position (bottom, or medium side up). Avoid freezing and overheating and minimize exposure to light. Do not open until ready to use. Allow the medium to warm to room temperature before inoculation.

Medium must be used before the expiration date.

The medium surface should be smooth, glistening, and free of excess moisture. Do not use plates if they have been frozen or show evidence of microbial contamination, discoloration, drying (e.g. cracked or wrinkled surface pulling away from the sides) or other signs of deterioration.

The Gono-Pak CO2 tablets and bags may be stored with the plates at 2–8°C or separately from the plates at ambient room temperature. Do not use Gono-Pak bags if they are perforated or defective or tablets if they appear to be damaged (broken tablet or torn foil).

Obtaining a Specimen

Swabs should be sterile and made of synthetic material i.e. not cotton or wood

****Take specimens for culture before specimens for NAAT****

Acceptable specimens:

Endocervix
Insert sterile polyester (Dacron) swab into endocervical canal and allow reasonable time, about 15-30 seconds, for secretions to absorb.

Urethra (female)
Strip the urethra toward its orifice to express exudate. Use a sterile calcium alginate mini-swab to obtain specimen.

Urethra (male)
Exudate expressed into the urethral meatus can be transferred to the selective culture medium with a sterile calcium alginate mini-swab. When exudate is not demonstrated, a specimen should be obtained using a calcium alginate mini-swab inserted 2-3 cm into the anterior urethra. Rotate swab, and leave it in place for at least 2 seconds to facilitate absorption.

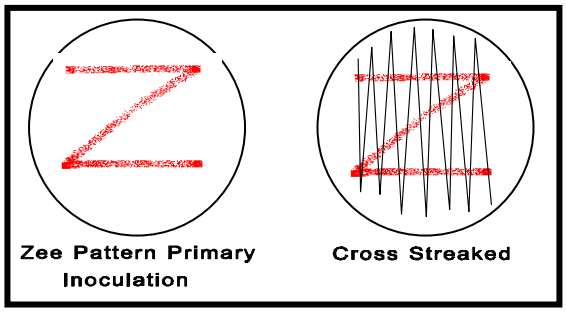
Anal Canal (male and female)
Insert sterile polyester (Dacron) swab approximately 1 to 1.5 inches into the anal canal beyond the anal sphincter and allow reasonable time, 15-30 seconds, for secretions to absorb. Gently rotate the swab to sample the anal crypts.

Throat (male and female)
Depress the tongue with a tongue depressor. Swab the posterior pharynx and tonsillar crypts and inflammed areas with a polyester (Dacron) swab being careful to avoid the tongue and uvula. While it is not necessary to make the patient gag, it is important to be sufficiently thorough get a good sample.

Male Pre-pubertal Child
Collect specimen from pre-pubertal male according to procedures described for adult males – except that the swab should be inserted no more than 1 cm into the urethra.

Female Pre-pubertal Child
Due to trauma involved, a vaginal speculum examination in a pre-pubertal female is not recommended to obtain a culture specimen. Obtain a specimen from vaginal vault by separating labia, manually exposing the introitus, and using a calcium alginate swab.

Inoculating the medium



Roll the swab between the finger and thumb in a large "Z" pattern on the medium to provide adequate exposure of swab to the medium for transfer of organisms. Cross-streak immediately with a second sterile swab.

Handling the Specimen

- Place Sunquest label on agar side of plate (i.e. not on the lid of plate)
- Place the culture plate in CO_2-enriched atmosphere right away by placing it in the polyethylene bag provided. Cut off the corner of one foil-wrapped CO2 tablet to expose the tablet and place in the bag. DO NOT ADD WATER TO THE TABLET.
- Seal the bag tightly.
- Put the sealed bag in incubator as soon as possible (within 15 minutes maximum) in an inverted position (i.e. agar bed up).
- If the incubator is only used for GC plates, set at 36°C +/- 1°C
- If the incubator is also to be used for Quantiferon testing, set at 37°C +/- 1°C.
- The temperature should be monitored daily (except weekends and holidays) and the result recorded on an Incubator Temperature and Maintenance Log

Transporting the Specimen

- Incubate the plates for overnight before transporting to the laboratory.
- Keep inoculated plates in the incubator until they are transported to the laboratory.
- Transport at room temperature. Do not use cold pack or refrigerate. Care should be taken to protect the culture from extreme heat or cold and to ensure delivery to the testing laboratory as rapidly as possible.

Ordering the test on Sunquest

Prompt	Sunquest entry	Translation	Notes
Test *RE prompt*	GCC	N. Gonorrhoeae Culture	
Specimen description* *SDES prompt*	**MUGS**	male urethral swab	preferred for males
	URSW	urethral swab	preferred for females
	URETH	urethra	
	THRT	throat	preferred code
	THR		
	RSW	rectal swab	preferred code
	RCT	rectal	
	RECT	rectal	
	CERV	cervix	
	VAG	vagina	
Reason for test *SREQ prompt*	TOC	test of cure	
	PABU	possible abuse (adult)	
	ABU	possible child abuse	
	TRFA	suspected treatment failure	
	;GISP	GISP	semicolon is required GISP is done at MLK and LAGLC only

Granuloma Inguinale (Donovanosis)

(Adapted from CDC 2006 STD Treatment Guidelines)

Granuloma inguinale is a genital ulcerative disease caused by the intracellular gram-negative bacterium *Klebsiella granulomatis* (formerly known as *Calymmatobacterium granulomatis*). The disease occurs rarely in the United States, although it is endemic in some tropical and developing areas, including India; Papua, New Guinea; central Australia; and southern Africa. Clinically, the disease is commonly characterized as painless, progressive ulcerative lesions without regional lymphadenopathy. The lesions are highly vascular (i.e., beefy red appearance) and bleed easily on contact. However, the clinical presentation also can include hypertrophic, necrotic, or sclerotic variants. The lesions might develop secondary bacterial infection or can coexist with other sexually transmitted pathogens.

A. Diagnosis

1. Physical findings
    a. Classic beefy-red, painless genital ulcers which progress over weeks to months.
    b. Absence of regional lymphadenopathy (although ulcerations may occur over the inguinal region, mimicking lymph node involvement).
2. Laboratory
    a. Tissue crush preparation or biopsy showing classic bipolar-staining Donovan bodies (not done at LA County clinics).
    b. Organism cannot be grown in standard culture media.

B. Treatment

A limited number of studies on Donovanosis treatment have been published. Treatment halts progression of lesions, although prolonged therapy is usually required to permit granulation and re-epithelialization of the ulcers. Healing typically proceeds inward from the ulcer margins. Relapse can occur 6–18 months after apparently effective therapy. Several antimicrobial regimens have been effective, but a limited number of controlled trials have been published.

All treatments should be for a minimum of 3 weeks and until all lesions have healed completely. Some specialists recommend the addition of an aminoglycoside (e.g. gentamicin 1mg/kg IV every 8 hours) to these regimens if improvement is not evident within the first few days of therapy.

Recommended Regimens

1. Doxycycline 100 mg PO bid for minimum of 3 weeks

Alternative Regimens

2. Azithromycin 1g PO weekly for minimum of 3 weeks; OR
3. Ciprofloxacin 750 mg PO bid for minimum of 3 weeks; OR
4. Erythromycin base 500 mg PO qid for minimum of 3 weeks; OR
5. Trimethoprim-sulfamethoxazole 1 double-strength tablet (160mg/800mg) PO bid for minimum of 3 weeks;

C. Sex Partners

Persons who have had sexual contact with a patient who has granuloma inguinale within the 60 days before onset of the patient's symptoms should be examined and offered therapy. However, the value of empiric therapy in the absence of clinical signs and symptoms has not been established.

D. Pregnancy

Pregnancy is a relative contraindication to the use of sulfonamides. Pregnant and lactating women should be treated with the erythromycin regimen, and consideration should be given to the addition of a parenteral aminoglycoside (e.g., gentamicin). Azithromycin might prove useful for treating granuloma inguinale during pregnancy, but published data are lacking. Doxycycline and ciprofloxacin are contraindicated in pregnant women.

E. HIV Infection

Persons with both granuloma inguinale and HIV infection should receive the same regimens as those who are HIV negative. Consideration should be given to the addition of a parenteral aminoglycoside (e.g., gentamicin).

Herpes

Genital herpes is caused by one of two DNA viruses, herpes simplex virus (HSV) type 1 or type 2. Most genital herpes is caused by HSV-2; however, approximately 20% of genital first episodes are caused by HSV-1. HSV-1 genital infections are associated with less frequent symptoms and shed virus less frequently than do HSV-2 genital Infections. Oral HSV-2 is rare.

In the general US population, 22% of adults over age 12 are infected with HSV-2. Ninety percent of people seropositive for HSV-2 are unaware of their infection, however, most have mild unrecognized disease and probably shed virus from the genital area intermittently. Among whites, 15% of men and 20% of women are HSV-2 seropositive. Among blacks, 35% of men and 55% of women are seropositive. Seropositivity increases with age, number of sexual partners, and HIV infection.

Most sexual transmission occurs when the index case is asymptomatic. The likelihood of herpes transmission to others declines with increased duration of infection as the frequency of occurrences and asymptomatic viral shedding decreases over time. Infection with HSV-1 may provide protection against having symptomatic disease, but does not protect against acquiring HSV-2 virus.

There is mounting evidence that genital herpes infection facilitates both acquisition and transmission of HIV.

A. Definition of types of infection:

1. First clinical episode:

    a) Primary
    - First infection with either HSV-1 or HSV-2 disease is more severe than recurrent disease or non-primary infection.

    b) Non-primary infection:
    - Newly acquired infection with HSV-1 or HSV-2 in an individual previously seropositive to the other virus.
    - Symptoms tend to be milder than primary infection.
    - 25% of patients with a first clinical episode of HSV-2 have had a prior asymptomatic primary infection, this is called “first episode of recurrent herpes”. Type specific antibody will be present when the patient presents and the severity of the episode is comparable to a recurrence.

2. Recurrent symptomatic infection: disease is usually mild and short in duration.

3. Asymptomatic infection:

    a) Serum antibody is present.

    b) There is no known history of clinical outbreaks.

    c) Up to two thirds of patients with HSV-2 antibodies and “asymptomatic” disease actually have recurrent mild symptoms.

B. Clinical Manifestations:

1. Primary infection is characterized by multiple lesions that are more severe, last longer, and have higher titers of virus than recurrent infections. Illness typically lasts 2-4 weeks.

    a) Often associated with systemic symptoms including fever, headache, malaise, myalgia, and urinary retention in 10% of women. These peak within 3-4 days of the onset of the lesion and gradually recede over the next 3-4 days.

    b) Local symptoms are predominately pain (95%), itching, dysuria (60%), vaginal (95%) or urethral (30%) discharge, and tender inguinal adenopathy (80%).

    c) Lesions last an average of 12 days. Full epithelialization takes 17-20 days.

    d) Primary HSV-cervicitis occurs in ~90% of primary HSV-2 infections and 70% of primary HSV-1 infections. Clinical differentiation from gonorrheal or chlamydial cervicitis is difficult, though ulceration suggests HSV.

2. Recurrent infection is milder, tends to be unilateral, and lasts 5-10 days without treatment.

    a) Prodrome (local tingling, irritation) in ~50% begins 12-24 hours before lesions. Sometimes lesions do not occur ("false prodrome").

    b) HSV-2 primary infection more likely to recur than HSV-1 primary infections.

    c) Recurrences are more frequent if primary episode was prolonged > 30 days.

3. Complications of genital infection:

    a) Aseptic meningitis:
    - More common in primary than in recurrent infection.
    - More common with HSV-2 than HSV-1.
    - More common in women than in men.
    - May be severe, requiring hospitalization and/or parenteral narcotics.
    - There are generally no neurologic sequelae.

    b) Other rarer complications include:
    - Stomatitis and pharyngitis.
    - Radicular pain, sacral paresthesias.
    - Transverse myelitis.

- Autonomic dysfunction: hyperesthesias, neurogenic bladder, constipation, and impotence.
- Disseminated (viremic) infection: occasional in patients with atopic eczema, pregnant women, impaired CMI, neonates. Can be a cause of fulminant hepatitis in immunosuppressed patients.
- Ocular involvement (more common with HSV-1).
- Herpetic whitlow (more common with HSV-1).

C. Diagnosis

1. History:

   a) Genital herpes causes a wide variety of symptoms ranging from classically painful vesicles/ulcers to the atypical, including: vaginal or urethral discharge, skin or mucosal fissures, dysuria, dysparenia, and non-specific itching, burning, or tingling of anogenital skin.

   b) Patients may present with a history of recurrent genital lesions which may or may not be painful.

   c) History of contact to a known infected partner is infrequent and not necessary for diagnosis.

2. Examination:

   a) Intact vesicles may be present and are strongly suggestive of HSV infection.

   b) If ulcers and not vesicles are present then an appropriate evaluation of any genital ulcers must be done before assuming that the patient has HSV infection despite a compatible history (refer to the genital ulcer section for details). When herpetic ulcers become confluent, they may present as a large, painful solitary ulcer that may be clinically indistinguishable from chancroid.

   c) Other suspicious signs may be; tender lymphadenopathy, fever, urethritis, cervicitis, skin or mucosal fissures.

   d) As clinical diagnosis alone is insensitive and nonspecific, laboratory confirmation is needed to confidently diagnose genital herpes infection.

3. Laboratory:

<u>Herpes tests available at LAC PHL are:</u>

   a) **PCR:** Highly sensitive and specific. Distinguishes between types 1 & 2. Direct testing of lesions suspicious for herpes should be performed using HSV PCR. As HSV PCR is a DNA test with increased sensitivity, samples from symptomatic areas without classic vesicle or ulcer should be collected for

testing, regardless of the age of the lesion. The PCR is not FDA approved but has been internally validated by LAC PHL. It is not approved for use-in medico-legal cases.

b) **Viral culture:** Highly specific (>99%) but not as sensitive as PCR. Viral recovery depends on age of lesion and proper collection technique. Most cultures will be positive within 24-72 hours, but are generally held by the laboratory for 5- 7 days. Culture distinguishes between types 1 & 2 and must be performed for medico-legal cases.

c) **HSV-2 type-specific serologic tests**:

- Detect antibodies specific to HSV-2 based on HSV-specific glycoprotein G2.
- Sensitivity ~93-99%; false negatives may occur, especially after early infection. The window period is not well documented and varies with different tests and among patients. At 6-12 week post-infection the sensitivity is 60%, at 12 weeks it is over 70%.
- Specificity 94-98%; false-positives can occur, especially in patients with low likelihood of HSV-2 infection and in patients with HSV-1 co-infection.
- HSV-2 serologic tests are indicated for the work-up of recurrent genital symptoms without detectable lesions, for patients with lesions suggestive of herpes whose PCR/culture is negative, and for screening in patients whose partners have herpes.
- Note that a true positive does not tell if person has had or will have symptoms, how long they have been infected or how frequently they will shed the virus.
- Note that a patient with a true negative HSV-2 serologic test could have a lesion due to HSV 1 (approx. 20% of genital herpes is caused by HSV-1 and over 50% in the USA are infected with HSV-1 in childhood).

<u>Work-up of genital symptoms:</u>

- If vesicles are present, HSV PCR should be performed to confirm diagnosis and determine HSV type.

- If genital ulcer(s) are present, HSV PCR of lesion should be performed as part of the work-up for GUD. This will confirm a genital herpes ulcer as well as determine the HSV type.

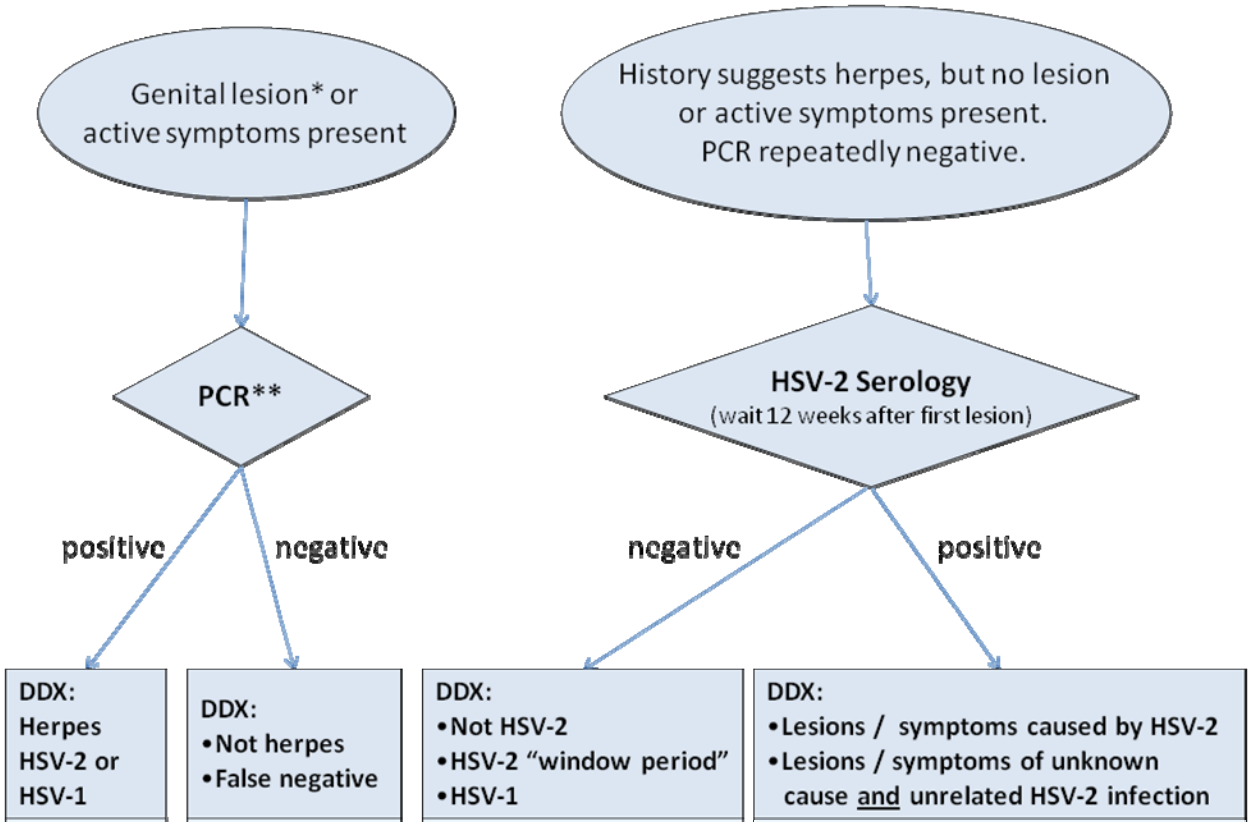
- Patients with symptoms of vaginitis or urethritis without clinical signs

supporting the diagnosis of vaginitis or urethritis should receive HSV PCR testing as part of a diagnostic work-up.

- Patients reporting history of recurrent genital lesions/symptoms but without active symptoms or signs at the time of clinic visit should be offered testing for HSV-2 antibodies and told to return to clinic when they develop active symptoms for direct testing of the lesion/symptoms.

- For medico-legal cases, request both culture and PCR, which can be run on same sample. Order both tests on MYSIS and label specimen with both accession numbers.

- See algorithm below for summary of work-up.



**Evaluation of new genital lesions should include syphilis screening with RPR, as well as screening for other STDs or HIV, depending on risk factors.*

**In medicolegal cases, if a lesion is present, culture should be performed (in addition to PCR).

Use a high index of suspicion for atypical or recurring lesions or symptoms (e.g. fissures, excoriations, recurrent vaginitis, cervicitis or urethritis of unknown etiology).

Note that this chart differs from the State Guidelines as PCR is available in LAC clinics.

Screening:

a) Screening persons with no history of symptoms of herpes is not indicated at LAC STD clinics unless they fit the following scenarios:
    - Patient's sex partner has known genital herpes
    - Patient is HIV infected

Diagnostic criteria:

a) Recovery of HSV by PCR or tissue culture confirms genital herpes and specifies HSV type.

b) A positive HSV-2 antibody test confirms current HSV-2 infection, however cannot diagnose the etiology of a lesion. As >95% of HSV-2 infections are anogenital, a diagnosis of genital herpes is appropriate and the patient should be counseled accordingly.

c) A positive HSV-1 antibody test (not currently available at LAC PHL) confirms current HSV-1 infection but cannot be used to diagnose genital herpes. Isolation of HSV-1 from a genital lesion is needed to confirm genital HSV-1 infection.

*d) T*ypical painful genital or anogenital lesion(s) and exclusion of other causes of genital ulcers should be presumptively treated and counseled as genital herpes. Appropriate laboratory confirmation should be pursued as outlined above in section *Work-up of genital symptoms.*

D. Treatment:

Overview: Antiviral therapy decreases duration of outbreaks, frequency of symptomatic recurrences, asymptomatic shedding and transmission to uninfected partners.

1. Treatment for Primary or Initial Genital HSV Disease

Patients with a first episode of herpes should receive anti-herpetic agents. Though many may present with mild clinical symptoms, they may later develop severe or prolonged symptoms without treatment. Treatment should be extended if healing is incomplete after 10 days.

Acyclovir 400 mg orally TID x 7-10 days

Other treatments, not on PH formulary

Famciclovir 250 mg orally TID x 7-10 days

OR

Valacyclovir 1 g orally BID x 7-10 days

2. Treatment for Recurrent Infection

Goals of treatment for patients with recurrent genital herpes are to:

- Improve psychological well-being and reduce psychosocial and psychosexual morbidity
- Enhance control of patient's disease
- Reduce asymptomatic and symptomatic viral shedding, and
- Decrease transmission of disease.

a) Antiviral therapy for recurrent herpes can be administered either episodically to abort, ameliorate, or shorten the duration of lesions or continuously as suppressive therapy to reduce the frequency of recurrences.

b) Episodic and suppressive therapy options should be discussed with all patients with confirmed symptomatic genital herpes infection. Patients for whom suppressive therapy should be strongly encouraged are those: with new genital herpes infections, with frequent recurrences, with a known un-infected partner (particularly a pregnant partner), co-infected with HIV, or with marked anxiety associated with outbreaks. Short-term suppressive therapy (e.g. 1-3 months) should also be considered for patients for whom a recurrence in the short-term would be problematic.

c) Anti-viral medications are not indicated for asymptomatic persons with positive HSV-2 serology.

Episodic therapy for recurrent genital herpes:

- Decreases healing time by 2 days
- Decreases pain by 1 day
- Decreases viral shedding by 2 days
- Aborts ~25% of lesions if taken during prodrome

a) Start treatment during the prodrome or within a day of onset of lesions, if possible.

b) Patient should be provided with a take-home supply of drug to self-treat future outbreaks. They should be instructed to initiate treatment as soon as symptoms begin.

Acyclovir 800 mg orally BID x 5 days

OR

Acyclovir 800 mg orally TID x 2 days

OR

Acyclovir 400 mg orally TID x 5 days

Other treatments, not on PH formulary

Famciclovir 125 mg orally BID x 5 days

OR

Famciclovir 1 gm orally BID X 1 day

OR

Famclicovir 500 mg orally once followed by 250 mg orally BID x 2 days

OR

Valacyclovir 500 mg orally BID x 3 days

OR

Valacyclovir 1 gm daily x 5 days.

Daily Suppressive Therapy (short or long term)

- STD Clinic physicians may prescribe suppressive therapy with acyclovir for 1-13 months for symptomatic genital herpes (if eligibility requirements met). After one year, patients should be re-evaluated for need for further treatment. After 2 years, patients should be prescribed episodic therapy unless HIV infected or with a known discordant (i.e. uninfected) sex partner.

- Short-term suppression should be considered for patients for whom a genital herpes recurrence in the short-term will be problematic. Examples of this include: a pregnant uninfected partner for whom the patient wants to maximize protection in the 3rd trimester, patient about to go on job interviews, pregnant patient wanting to decrease risk of an outbreak at delivery (best done in conjunction with patient's ob-gyn).
- Eligibility requirements for suppressive therapy in LAC STD clinics are:
    - History consistent with clinical picture of genital herpes
    - Laboratory documentation of herpes infection
    - Exclusion of current renal disease by history
    - Patient is willing and able to take daily BID medication to decrease the frequency, severity, and/or risk of transmission of herpes.
    - No "medical home" identified to provide suppressive therapy (for long-term suppression only).
- Reduces the frequency of symptomatic genital herpes recurrences by 70% - 80% among patients who have frequent recurrences (i.e. ≥ 6 recurrences per year), and many patients report no symptomatic outbreaks.
- Reduces risk of transmission to uninfected sexual partners by ~50%.
- Decreases anxiety among patients who report marked anxiety/depression associated with a new diagnosis or with recurrent symptoms of genital herpes.

Additional considerations:

- Frequency of outbreaks diminishes after first 2 years of infection as does psychological adjustment to the disease.
- Suppressive therapy will not eradicate latent virus or change the frequency or severity of recurrences when it is discontinued.
- Suppression is not usually necessary for HSV-1.

Typical suppressive regimens are as follows:

Acyclovir 400 mg orally BID

Other treatments, not on PH formulary

Famciclovir 250 mg orally BID

OR

Valacyclovir 500 mg orally once a day

OR

Valacyclovir 1 gm orally once a day (should be chosen over 500 mg dose for patients with ≥ 10 episodes/year)

E. Pregnancy

Known history of genital herpes:

Women with a history of genital herpes can deliver their infants vaginally if no lesions are present at delivery. Women with recurrent infection are at much lower risk for transmission of the virus to the neonate during vaginal delivery than women with primary infection during delivery. The risk of perinatal transmission during a vaginal delivery in women with genital recurrences is <1%. C-sections are not indicated unless patient has herpes lesions at delivery.

Acyclovir, Famciclovir and Valacyclovir are all FDA pregnancy category (B). However, as there is more data on acyclovir use in pregnancy, some experts recommend acyclovir as the drug of choice if treatment is given during pregnancy. First episode genital herpes in pregnant women may be treated with oral acyclovir. For women with recurrent genital herpes, some experts recommend herpes suppression during third trimester of pregnancy to reduce the risk of a genital herpes recurrence during delivery and therefore reduce the risk of c-section and the possible risk of neonatal herpes. Patients with genital herpes should be referred to their prenatal provider for management.

Screening in pregnancy

Women at greatest risk of transmitting herpes to infants are uninfected pregnant women who acquire herpes late in pregnancy, before acquiring HSV 1 or 2 antibodies. The risk of perinatal transmission during a vaginal delivery in a woman with primary infection is approximately 30-50%. Pregnant patients in whom an HSV infection is diagnosed should inform their obstetrician. Primary genital HSV-I infection can occur in pregnant women and receptive oral sex should be avoided.

Screening for type-specific herpes antibodies is not recommended in pregnancy unless the current sex partner is infected with herpes. The goal of screening is to identify uninfected pregnant women to counsel them to decrease their risk of acquiring genital herpes (HSV 1 or 2) during pregnancy.

Pregnant women with sex partners known to have herpes should be evaluated for symptoms and signs of herpes. If symptoms or signs are present, the lesion should be swabbed for PCR testing. If there are no symptoms or signs serological testing for HSV-2 should be offered. Serodiscordant couples should be advised to avoid any oral (if partner has orolabial HSV 1 infection) or genital contact—particularly during the final trimester of pregnancy. As HSV-1 testing is not available at LAC STD clinics, pregnant women with known HSV-1 infected partners (oral or anogenital) should be educated to avoid any genital contact with their infected partner during the third trimester.

Suppressive therapy should be offered to symptomatic infected partners to further reduce the risk of transmission to pregnant women, who are not known to have herpes. This should only be done in conjunction with education, advising consistent condom use and abstinence when lesions are present, as suppressive therapy only reduces transmission risk by half.

F. HIV Infection

HIV can increase the severity and duration of herpes symptoms. Longer courses of therapy may be needed for treatment of recurrences and higher doses may be needed for suppression. HIV infected persons are likely to be more contagious for herpes (and perhaps HIV) due to more frequent symptomatic and asymptomatic viral shedding.

Acyclovir resistance does occur in this population and should be suspected with lesions that persist or recur despite appropriate antiviral treatment. These patients should be managed in consultation with an HIV specialist. If you suspect acyclovir resistance, collect specimen for herpes culture and send to LA PHL. PHL director needs to be contacted at 562-658-1333 to determine appropriate special testing.

Recommended Regimens for Daily Suppressive Therapy in Patients with HIV

Acyclovir 400-800 mg orally BID-TID

Other treatments, not on Public Health formulary

Famciclovir 500 mg orally BID

OR

Valacyclovir 500 mg orally BID

Recommended Regimens for Episodic Infection in Patients with HIV

Acyclovir 400 mg orally TID for 5-10 days

Other treatments, not on PH formulary

Famciclovir 500 mg BID for 5-10 days

OR

Valacyclovir 1 g orally BID for 5-10 days

F. Acyclovir Allergies

Acyclovir allergy is generally rare. However, for allergic patients, treatment options are limited. Valacyclovir and famciclovir may not be offered as alternatives as they may cross-react and cause allergic reactions. Other anti-herpes medication is available but only in intravenous form with toxic side effect profiles. For allergic patients with severe and frequent outbreaks, a referral to an allergy/immunology specialist and an infectious diseases specialist is recommended for further evaluation and treatment.

G. Follow-up

As a new diagnosis of genital herpes can cause much confusion and anxiety among patients and their partners, all patients newly diagnosed with genital herpes should be offered a follow-up appointment for education and counseling.

Patients in whom a presumptive diagnosis has been made during the initial evaluation of a genital ulcer must return in one week for a follow-up evaluation.

H. Counseling/Education

Key points when the patient first presents with suspected genital herpes. Patients should:

a) Understand how to take prescribed oral medications.

b) Keep the lesions clean and dry.

c) Avoid sex while lesions are present.

d) Return for results and further information about herpes.

At follow-up visit explain test results and cover the counseling points (below), adapted from CDC 2010 STD Treatment Guidelines.

Counseling of infected persons and their sex partners is critical to the management of genital herpes. The goal of counseling is to 1) help patients cope with the infection and 2) prevent sexual and perinatal transmission. Although initial counseling can be provided at the first visit, many patients benefit from learning about the chronic aspects of the disease after the acute illness subsides. Multiple resources are available to assist patients and their partners including: the LAC STD Program Health Education hotline 1-800-758-0880 and ASHA www.ashastd.org

Specific counseling messages for all patients with clinical or serologic diagnosis of HSV-2 infection should include the following information:

- Information about the natural history of the disease, with emphasis on the potential for recurrent episodes, asymptomatic viral shedding, and attendant risks of sexual transmission.

- Information about episodic or suppressive treatment with antiviral medication to shorten the duration of or prevent symptoms. Many persons might prefer suppressive therapy, which has the additional advantage of decreasing the risk for genital HSV-2 transmission to susceptible partners.

- All patients with genital HSV infection should be encouraged to inform their current sex partners that they have genital herpes and to inform future partners before initiating a sexual relationship.

- Persons with genital herpes should be informed that sexual transmission of HSV can occur during asymptomatic periods. Asymptomatic viral shedding is more frequent in genital HSV-2 infection than in genital HSV-1 infection and is most common in the first 12 months following acquisition of HSV-2, but may persist for years, less frequently, in some individuals.

- Patients should be advised to abstain from sexual activity when lesions or prodromal symptoms are present.

- Latex condoms, when used consistently and correctly, can reduce the risk for genital herpes when the infected areas are covered or protected by the condom. Because condoms do not cover all exposed areas, they are likely to be more effective in preventing infections transmitted by fluids from mucosal surfaces than in preventing those transmitted by skin-to-skin contact (e.g., HSV).

- The risk of HSV-2 sexual transmission may be decreased by daily suppressive therapy.

- Sex partners of infected persons should be advised that they may themselves be infected even if they have never experienced symptoms. Type-specific serologic testing of asymptomatic partners of persons with genital herpes can determine whether they are at risk for HSV acquisition.

- The risk of neonatal infection should be explained to all patients, including men.

- Pregnant women and women of childbearing age who have genital herpes should inform their providers who care for them during pregnancy, as well as those who will care for their newborn infants.

- Pregnant women who are not infected with HSV-2 should be advised to avoid intercourse during the third trimester with men who have genital herpes. Similarly, pregnant women who are not infected with HSV-1 should be counseled to avoid genital exposure to HSV-1 (e.g., cunnilingus with a partner with oral herpes) during the third trimester.

- Patients with a positive HSV-2 serologic test should be taught to recognize the common manifestations of genital herpes. Antiviral therapy is not recommended for patients without clinical manifestations of infection.

- HSV-2 infections are associated with a significantly increased risk of acquiring HIV. Infected people should be educated about their increased risk of HIV acquisition and should protect themselves against HIV, as well as prevent HSV transmission to partners. Patients should be informed that suppressive antiviral therapy does not reduce the increased risk for HIV acquisition associated with HSV-2 infection.

I. Evaluation of Sex Partners

Sex partners of patients with HSV infection may benefit from counseling and evaluation including HSV-2 serologic testing if no lesions amenable to direct testing.

Appendices (on STD Program intranet page)

- Chronic Suppression of Herpes Simplex Virus Type 2 (HSV-2) Policy 313
- Giving Patients a Record of Their Positive Herpes Result
- Herpes Testing - Patient Information Leaflet B518 (English)
- Herpes Testing - Patient Information Leaflet B518S (Spanish)
- New Method of Testing for Herpes Simplex Virus (PHL letter)

HIV Testing

It has been well-documented that STDs can contribute to the transmission or acquisition of the human immunodeficiency virus (HIV). Providing STD clinic patients with HIV testing services is an important part of STD care.

A. Screening for HIV Infection

The Centers for Disease Control and Prevention (CDC) recommends that the following populations are screened for HIV: 1) patients age 13-64 in all health-care settings, unless they decline (opt-out screening), 2) persons at high risk for HIV infection (screen at least annually), 3) pregnant women (opt-out screening as part of routine prenatal screening) and 4) all patients initiating treatment for TB. In addition, all patients seeking treatment for STDs, including all patients attending STD clinics, should be screened routinely for HIV during each visit for a new complaint, regardless of whether the patient is known or suspected to have specific behavior risks for HIV infection.

In the United States, the Enzyme-linked Immunoassay (EIA) is the most common screening test used to look for antibodies to HIV in blood, oral fluid, and urine. Currently, the LAC Public Health Laboratory uses an HIV 1/2 Chemiluminometric immunoassay (CIA) for screening serum and oral fluid for HIV antibodies. Like the EIA, the serum CIA has a high sensitivity (100%) and specificity (99.9%). However, it is important to emphasize that all reactive screening tests must be confirmed with a supplemental test i.e. Western blot, Indirect immunofluorescence assay (IFA) or HIV-1 RNA assay before a diagnosis of HIV can be made. The PHL uses the Western blot test for confirmation.

Window Period and Early Detection with CIA
Following infection, HIV-specific antibodies are produced. However, the timing of such antibody production depends on host and viral characteristics. Antibodies may be present early in infection but below the limit of detection for some assays. The window period for the CIA used at the PHL is approximately four weeks after infection, although there is a wide range, including some instances of extremely delayed seroconversion. Patients with recent exposures who test negative should be advised to re-test three months after their last potential exposure to HIV (the 'window period').

Interpreting HIV CIA (and EIA) Results

Non-reactive CIA Results
A non-reactive CIA indicates no HIV antibodies and can be interpreted as no HIV infection. This result does not require confirmatory testing.

If the patient is still in the window period, they should be offered re-testing three months after their last potential exposure to HIV. If acute HIV infection is suspected, then a viral load should be ordered to assess for presence of virus in the blood (see appendix A).

Reactive CIA Results
A reactive CIA indicates the possibility of HIV infection and requires confirmatory testing. If a sample tests reactive on CIA, the PHL will automatically repeat the CIA and perform a Western blot (see below).

Indeterminate CIA Results:
Indeterminate tests should be considered on a case-by-case basis. All such tests will be repeated by the lab. If persistently indeterminate, a Western blot will be performed by the lab automatically.

Rapid HIV Tests:
Rapid HIV tests detect HIV antibodies and can yield results in approximately 20 minutes. In the community, it is common to see tests performed on whole blood (fingerstick or venipuncture) and on oral fluid (see appendix B). Although rapid testing is not used in the LAC STD clinics, patients may be referred to clinic following one of these tests.

In low-prevalence populations an increased rate of false-positive results can occur when utilizing rapid testing methods. This has been particularly noted with oral-fluid rapid HIV tests. This serves as a reminder that all rapid HIV tests, and oral-fluid-based ones in particular, if initially positive, must be confirmed.

B. Confirmation of HIV Infection with Western Blot (WB)
All reactive screening tests in the STD clinic must be confirmed with WB to prevent giving patients a false positive diagnosis of HIV.

The WB result is reported as "bands" of antibodies to the following viral proteins: gp160, gp120, p66, p55, p51, gp41, p31, p24, p17, and p15. The "gp" refers to glycoproteins and "p" indicates the proteins associated with the virus. It may take five weeks or more after HIV infection before a positive WB may develop.

Interpretation of WB Results:

Positive WB Result:
The CDC guidelines require the presence of *at least two* of the following bands: p24, gp41, gp120 or gp160 for a positive result classification. A positive result means that the patient is HIV-infected. Some authorities would consider one band present from *each* of the following two sets of bands to be a positive result:

1. p24 or p35
2. gp 41, gp120, gp 160

Negative WB Result:
A negative result is considered to be the absence of all bands. It indicates that the patient is not considered to be infected with HIV, and the HIV CIA test was falsely positive. Re-test in three months if in the window period. However, if clinical suspicion is high for acute infection, a viral load test may be considered.

Indeterminate WB Result:
An indeterminate classification occurs when one or more bands are present but do not fulfill the criteria for a positive test.

- Patients with recent HIV exposure and/or who are suspected to be undergoing HIV seroconversion: an HIV viral load is recommended to assess for presence of virus in the blood. If the viral load is positive, then the patient is likely to be HIV infected. If the viral load is negative, the patient is not likely to be infected. Repeat CIA testing in one month.
- If the patient does not appear to be at high risk for HIV infection: a viral load can be performed or the CIA and WB can be repeated in one month. Patients with continued indeterminate WBs over six months in the absence of any known risk factors are unlikely to be HIV-infected and considered to be "stable indeterminates."

Non-specific Banding WB Result:
A non-specific banding result is reported when non-viral bands are reported by the laboratory. Such individuals are not likely to be HIV-infected but should be re-tested with a CIA in one month as a precaution. If the repeat CIA is reactive, then another WB will be run. If the WB continues to show only non-specific banding upon repeat testing, the patient is not likely to be infected.

C. Viral Load Testing

Viral load tests measure the amount of virus present in the serum and are often used to monitor the activity of the virus and the level of control being achieved by anti-retroviral therapy (if the individual is taking such medications). While viral load testing is not used for routine HIV screening by PHL, it can be useful in situations when conventional testing does not yield definitive results or when acute infection is suspected. The presence of HIV can be detected as early as one to two weeks after infection but may take longer in some individuals.

It is important to keep in mind that, depending on the pretest probability and population screened, viral load testing carries a false positive rate of up to 5-9%. Results of a viral load test which would be suggestive of primary or acute HIV infection would be $\geq$100,000 copies/mL and often >1,000,000 copies/mL. Patients with positive viral load results should have repeat CIA testing with WB until seroconversion occurs, to confirm the HIV diagnosis.

Viral load testing should only be ordered when clinically indicated. This test also requires special specimen handling – see appendix A for details on the appropriate collection tube, specimen handling and transport.

D. Recognizing Acute HIV Infection

Primary or acute HIV infection occurs two to four weeks after infection with HIV and can present like the flu or other viral illness. In general, 50-80% of those infected develop symptoms of acute HIV. Of those diagnosed with acute HIV, 50% of patients were seen at least three times by a health care provider before the diagnosis. In an acute HIV detection study done by Los Angeles County STD Program between February 2006 and March 2008, of 43 patients diagnosed with acute HIV, approximately 25 (58%) presented with acute HIV and STD symptoms and 40 (93%) were MSM or MSM/W. This demonstrates the importance of recognizing the symptoms of acute HIV infection in order to make the diagnosis. Due to the epidemiology of acute HIV in LAC, acute HIV should be considered in MSM with the following symptoms:

- Decreased appetite
- Fatigue
- Fever
- Headache
- Malaise
- Swollen lymph nodes
- Muscle stiffness or aching
- Rash
- Sore throat
- Ulcers of the mouth and esophagus

These symptoms can last from a few days to four weeks, and then resolve.

If acute HIV is suspected, then a viral load in addition to the CIA should be ordered to assess for presence of virus in the blood. Persons suspected of recently acquired HIV infection should be referred for immediate consultation with an HIV specialist

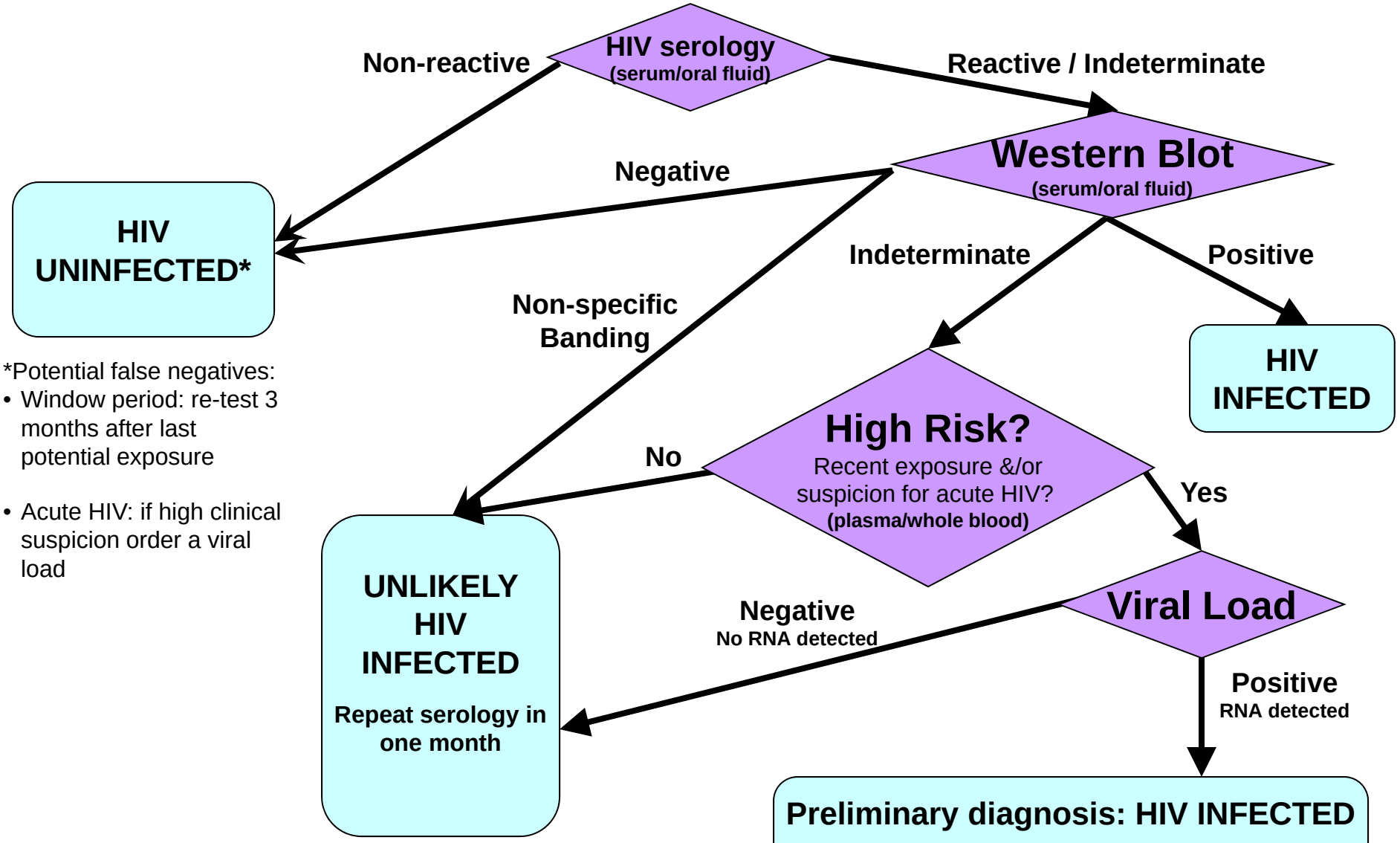
E. Reporting

HIV cases should be reported to the HIV Epidemiology Program on form DPH 8641. The form and further information is available at http://publichealth.lacounty.gov/hiv/index.htm or by calling the HIV Reporting Help Desk at (213) 351-8516.

F. Partner Counseling and Referral Services (PCRS)

PCRS should be offered to all newly diagnosed HIV patients. See OAPP HIV testing and counseling training manual for further information on the management of patients with newly diagnosed HIV infection.

LA County DPH - STD Clinic HIV Testing Algorithm[1]



*Potential false negatives:

- Window period: re-test 3 months after last potential exposure
- Acute HIV: if high clinical suspicion order a viral load

[1]Algorithm to be used in conjunction with text

Appendix A

HIV Viral Load Specimen Requisition, Collection and Handling Instructions

Specimen requisition:
The SUNQUEST ordering code for HIV Viral Load Testing is VLT.

Specimen collection:
Collect the patient's blood in K2EDTA tube (lavender top). Do not use glass vacutainers and fill the tube completely.

Note, if no centrifuge is available and under special circumstances, HIV viral load may be performed using whole blood after proper laboratory notification.

Specimen handling:
Clinics with centrifuges and skilled personnel:

1. Centrifuge the specimen to separate plasma from whole blood within 6 hours.
2. Once the specimen has been spun down, use a pipette to transfer at least 3ml of plasma to a sterile screwcap polypropylene aliquot tube. Ensure that the tip of the pipette does not touch the clot at the bottom of the tube.
3. Deliver to lab in a separate container on an ice pack as soon as possible. If necessary the sample may be stored in a refrigerator at 2-8°C for up to 5 days but the earlier it is tested the better.

Clinics without centrifuges:

1. Immediately after collecting the specimen, call the Public Health Laboratory central accessioning at (562) 658-1460 to alert them that a HIV viral load specimen is on its way and to arrange courier scheduling.
2. If sample is not centrifuged, it must reach the lab by 3 pm in the afternoon. When sending the specimen, place it in a separate delivery container, store/transport at 2-8°C, and clearly mark the container with "VIRAL LOAD STAT PLEASE DELIVER TO VIRAL LOAD SECTION ASAP". ***If the sample arrives too late, it will be rejected.***

Equipment:

- K2EDTA tube (lavender top) – available from PHL as a 'write-in' on the requisition form
- 5ml pipettes
- Sterile screwcap polypropylene aliquot tube (Market Lab catalog # ML5368 and #ML5370)

Appendix B

FDA-Approved Rapid HIV Antibody Screening Tests

February 4, 2008

	FDA Approval Received	Specimen Type	CLIA Category*	Sensitivity** (95% CI)	Specificity** (95% CI)	Manufacturer	Approved for HIV-2 Detection?	List Price Per Device^	External Controls
OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	Nov 2002	Oral fluid	Waived	99.3% (98.4-99.7)	99.8% (99.6-99.9)	OraSure Technologies, Inc. www.orasure.com	Yes	$17.50	Sold Separately ($25 each)
		Whole Blood (finger stick or venipuncture)	Waived	99.6% (98.5-99.9)	100% (99.7-100)				
		Plasma	Moderate Complexity	99.6% (98.9-99.8)	99.9% (99.6-99.9)				
Uni-Gold Recombigen HIV	Dec 2003	Whole blood (fingerstick or venipuncture)	Waived	100% (99.5-100)	99.7% (99.0-100)	Trinity Biotech www.unigoldhiv.com	No	$15.75 *$8.00•*	Sold Separately ($26.25 each)
		Serum & Plasma	Moderate Complexity	100% (99.5-100)	99.8% (99.3-100)				
Reveal G-3 Rapid HIV-1 Antibody Test	Apr 2003	Serum	Moderate Complexity	99.8% (99.2-100)	99.1% (98.8-99.4)	MedMira, Inc. www.medmira.com	No	$14.00	Included
		Plasma	Moderate Complexity	99.8% (99.0-100)	98.6% (98.4-98.8)				

•*"Public health" price for public health programs that are recipients of CDC funds for expanded HIV testing*
* Clinical Laboratory Improvement Amendments: CLIA regulations identify three categories of tests: waived, moderate complexity, or high complexity
** Sensitivity is the probability that the test result will be reactive if the specimen is a true positive; specificity if the probability that the test result will be nonreactive if the specimen is a true negative. Data are from the FDA summary basis of approval, for HIV-1 only. For HIV-2 information, see package inserts.
^ Actual price may vary by purchasing agreements with manufacturers
Note: Trade names are for identification purposes only and do not imply endorsement. This information was compiled from package inserts and direct calls to manufacturers.

Prepared by Kali Stanger & Frances Margolin at HRET; Margaret Lampe, Jill Clark, and Bernard Branson at CDC.

Appendix B

FDA-Approved Rapid HIV Antibody Screening Tests

February 4, 2008

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MultiSpot HIV-1/HIV-2 Rapid Test	Nov 2004	Serum	Moderate Complexity	100% (99.94-100)	99.93% (99.79-100)	BioRad Laboratories www.biorad.com	Yes – differentiates HIV-1 from HIV-2	$25.00	Included
		Plasma	Moderate Complexity	100% (99.94-100)	99.91% (99.77-100)				
Clearview HIV 1/2 STAT-PAK	May 2006	Whole Blood (finger stick or venipuncture)	Waived	99.7% (98.9-100)	99.9% (99.6-100)	Inverness Medical Professional Diagnostics www.invernessmedicalpd.com	Yes	$17.50 *$8.00•*	Sold Separately ($50/set)
		Serum & Plasma	Non-waived	99.7% (98.9-100)	99.9% (99.6-100)				
Clearview COMPLETE HIV 1/2	May 2006	Whole Blood (finger stick or venipuncture)	Waived	99.7% (98.9-100)	99.90% (99.6-100)	Inverness Medical Professional Diagnostics www.invernessmedicalpd.com	Yes	$18.50 *$9.00•*	Sold Separately ($50/set)
		Serum & Plasma	Non-waived	99.7% (98.9-100)	99.9% (99.6-100)				

• "Public health" price for public health programs that are recipients of CDC funds for expanded HIV testing

* Clinical Laboratory Improvement Amendments: CLIA regulations identify three categories of tests: waived, moderate complexity, or high complexity

** Sensitivity is the probability that the test result will be reactive if the specimen is a true positive; specificity if the probability that the test result will be nonreactive if the specimen is a true negative. Data are from the FDA summary basis of approval, for HIV-1 only. For HIV-2 information, see package inserts.

^ Actual price may vary by purchasing agreements with manufacturers

Note: Trade names are for identification purposes only and do not imply endorsement. This information was compiled from package inserts and direct calls to manufacturers.

Prepared by Jeanette Lyons & Frances Margolin at HRET; Margaret Lampe, Jill Clark, and Bernard Branson at CDC.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is a systemic sexually transmitted disease caused by serovars (sub-types) L1, L2, or L3 of Chlamydia trachomatis. It presents in a variety of clinical syndromes and is commonly characterized by proctitis / proctocolitis or the bubonic form with tender inguinal lymphadenopathy.

In the past LGV was considered an endemic infection in Africa, Southeast Asia, Central and South America, and the Caribbean. In other regions of the world, LGV was sporadic and uncommon. Since 2004, there have been a number of LGV outbreaks reported throughout Europe, most notably in the Netherlands, and in the U.S. (San Francisico), predominantly among men who have sex with men (MSM). The risk factor for transmission was primarily unprotected anal intercourse. Signs and symptoms of proctitis were observed at a high frequency, while presentation with genital ulceration and tender inguinal lymphadenopathy was rare.

LGV should be considered in those at risk for sexually transmitted diseases – especially MSM and those reporting unprotected anal intercourse – who present with rectal complaints or a tender lymphadenopathy syndrome.

A. Clinical Presentation:

The clinical presentation of LGV can vary and the incubation period is 3 to 12 days or longer. Primary LGV infection may present as a small genital papule that may ulcerate, although the ulcer is generally painless and heals very rapidly. Because of the transient nature of the ulcer, recent case series suggest that patients are rarely identified at this stage. Untreated infection extends to lymph nodes and commonly presents as tender lymphadenopathy with or without subsequent bubo (inflamed, purulent lymph node) formation. The average time to development of this stage is 10 to 30 days since infection, but it may be delayed for as long as 4 to 6 months. The bubo is unilateral in two-thirds of cases and may enlarge to the point of rupture with the development of sinus tracts that drain for weeks or months before healing. Genital and colorectal LGV lesions might also develop secondary bacterial infection or might be co-infected with other sexually and non-sexually transmitted pathogens.

The most common clinical manifestation of LGV among heterosexuals is tender inguinal and/or femoral lymphadenopathy that is typically unilateral.

The proctitis syndrome, following rectal exposure in women or MSM might result in mucoid and/or hemorrhagic rectal discharge, anal pain, constipation, fever, and/or

tenesmus. The painful inflammation can progress to proctocolitis. Rare complications of LGV include chronic inflammation with development of genital elephantiasis, fistulas, and rectal strictures, sometimes requiring surgical intervention.

B. Diagnosis, treatment, management of sex partners and reporting:
See algorithm.

Detection and Management of LGV in LA County DPH STD Clinics

Rectal discharge, bleeding, pain on defecation or tenesmus

- **Perform anoscopy** to visualize & swab lesions
- **If no lesions present:** swab rectal wall.
- **If anoscopy unavailable**: collect blind rectal swab

- Send rectal swab for Chlamydia NAAT [MISYS code ACRTS] as per routine for CT/GC NAAT

Tender lymphadenopathy or bubo with or without genital ulcer

- **If genital ulcer or draining lymph node:** swab site(s).
  - Use a dacron tipped swab
  - Place in M4RT transport media.
  - Send for chlamydia culture [MISYS code CT] in a biohazard bag on cold pack or wet ice to Public Health Lab ASAP (within 24 hrs of collection).

ADDITIONAL TESTS*

In addition to swab(s) above, patients should also have appropriate STD evaluation and treatment per standard protocol for HIV, syphilis, herpes, chlamydia, gonorrhea, and/or chancroid.

INITIATE LGV THERAPY**

- **Rx** Doxycycline 100 mg po BID x 21 days OR Erythromycin base 500 mg po QID x 21 days
- **Advise to abstain** until treatment completed
- **Clinical follow-up** at 1 wk & 1 month
- **Notify** LA County STD Program within 24 hrs using CMR Form

INITIATE PARTNER MANAGEMENT SERVICES for sex contact(s) in past 60 days (or last sex contact if >60 days)

- **Evaluate and treat symptomatic contact(s)** for LGV with above algorithm
- **Treat asymptomatic contact(s)** with Azithromycin 1g po x 1 OR
  Doxycycline 100 mg po BID x 7d
- **Advise contact(s) to abstain** until treatment is complete

NOTES:

* Due to concerns regarding the specificity and cut off values for the MIF, this test is no longer recommended in the diagnosis of LGV and is not available through the LA County Public Health Laboratory. In addition, the LGV PCR for CT-positive rectal NAATs and genital ulcer/lymph node cultures are no longer available through the Centers for Disease Control and Prevention.

** All suspected LGV cases should be treated presumptively.

For questions or concerns contact Dr. Christine Wigen at ph (213) 744-3070 or cwigen@ph.lacounty.gov

Molluscum Contagiosum

Molluscum contagiosum, caused by a poxvirus, is characterized by smooth, spherical papules with umbilicated centers that emerge on the skin of the genitalia, the thighs, the lower abdominal wall, and occasionally, the face. It has an average incubation period of two to three months (range one week to six months). Most lesions heal spontaneously, without scarring. However, lesions may persist for 2 to 3 months; infection may persist for several years. Transmission is through direct contact.

A. Diagnosis

1. History:

   Most patients are asymptomatic or present with a complaint of a rash or a "bump" or "warts."

2. Examination:

   a. The lesions are typically smooth spherical papules with pearly borders and a characteristic central umbilication. The core consists of caseous fluid or a keratotic plug. They are usually found on the aforementioned areas.

   b. The remainder of the exam is usually normal.

3. Laboratory:

   There is no specific laboratory test available to diagnose *molluscum contagiosum.*

4. Diagnostic criteria:

   a. Typical papules.

   b. Expression of a firm keratotic plug which may be followed by brisk bleeding.

B. Treatment

The benefits of treatment are uncertain. Lesions may heal spontaneously. Patients may also be instructed to squeeze the central plug of the lesions to expedite healing. For more extensive lesions, cryotherapy with liquid nitrogen may be used. It is used in the same manner as used with warts.

C. Follow-up

Patients may return at intervals of one to two weeks until lesions have disappeared and the skin has healed.

D. Counseling/Education

Patients should:

1. Return for evaluation if symptoms persist or recur after treatment;
2. Avoid intimate (direct) contact until lesions have disappeared.

E. Special Considerations

Extensive molluscum, repeated recurrence after treatment or appearance of lesions on the face are common in patients with cellular immunodeficiency and should raise the suspicion of HIV infection.

Pubic Lice (Crabs)

Crab lice, *Phthirus pubis,* usually infest the hairy parts of the pubic area but may also infest facial hair and eyelashes. Hairy men may have crab lice ascend onto the chest and axillary hair. Typically, crab lice are transmitted between sexual partners; rarely, they may be transmitted by sharing clothing, bedding, etc. Lice deposit nits (eggs) on the hair shaft; nits hatch in one week. Lice are sexually mature in eight to ten days and take blood meals from the skin in the pubic area, resulting in itching and excoriation. Secondary infection with skin pathogens (staph. or strep.) may occur.

A. Diagnosis

1. History:
   a. Patients generally present with pruritus in the pubic region.
   b. Often, patients have been able to visualize the lice or the nits.
2. Examination:
   a. The pubic hair should be carefully examined for the presence of lice and/or nits.
   b. Excoriation may be present but otherwise the skin should appear normal.
3. Laboratory:
   a. No specific laboratory tests are indicated.
4. Diagnostic criteria:
   a. Identification of lice or nits either grossly or microscopically attached to genital hairs.
   b. Pruritic erythematous macules or papules or secondary excoriations in the genital area and sexual exposure or close physical contact to a person infested with pubic lice.

B. Treatment

All treatments should be followed by combing the affected area with a fine-toothed comb.

Recommended

- Permethrin (1%) creme (Nix) rinse applied to the affected area and washed off after 10 minutes

  or

- Pyrethrins and piperonyl butoxide (RID, Triple X, A-200) applied to the affected area and washed off after 10 minutes.

C. Treatment in Pregnancy

Pregnant and lactating women should be treated with either permethrin or pyrethrins with piperonyl butoxide.

D. Follow-up

Patients should be re-evaluated after one week if symptoms persist. Re-treatment may be necessary if lice are found or nits are observed at the hair-skin junction. Reported resistance to pediculicides has been increasing and is widespread. See STD treatment guidelines for alternative treatment options, which are not on the PH formulary.

E. Counseling/Education

Patients should:

1. Understand how to apply prescribed medication;
2. Return after one week for evaluation if symptoms persist;
3. Refer sex partner(s) for treatment; and
4. Avoid sexual contact for at least 7 days and until partner(s) are treated.

F. Evaluation of Sex Partners

Individuals with sexual or close physical contact in the previous month should be referred for treatment.

G. Special Considerations

Clothing, bed linens, and towels should be washed and dried by machine (hot cycle in each) or dry-cleaned. Articles that cannot be washed or dry-cleaned can be sealed in a plastic bag and placed in storage for 72 hours.

Pediculosis of the eyelashes should be treated by the application of occlusive ophthalmic ointment or vaseline to the eyelid margins, twice daily for ten days to smother lice and nits.

Scabies

The itch mite, Sarcoptes scabiei, usually penetrates the skin, creating visible papules, or small, linear burrows, which contain the mites and their eggs. Common sites of infection include the flexor surface of the wrists, webbing between fingers, anterior axillary folds, the inner aspects of the upper thigh, and the belt line. Nodules appearing on the scrotum and penis typically are large. Scabies is rarely found on the head in adults. Two to six weeks after infection, pruritus (which is usually worse at night) begins. The itching represents a hypersensitivity reaction to the mite and will persist even after mites are dead. Individuals with a prior history of scabies may have more rapid onset of symptoms due to prior sensitization and symptoms can occur within 24 hours. Complications include secondary infections due to scratching.

Crusted scabies (i.e., Norwegian scabies) is an aggressive infestation that usually occurs in immunodeficient, debilitated, or malnourished persons. Crusted scabies is associated with greater transmissibility than scabies.

A. Diagnosis

1. History:
    a. Patients complain of a pruritic rash.
    b. Classically, the pruritus is so severe that it wakes the patient at night. If it is not worse at night, another diagnosis should be considered.
    c. There may be known contact to a partner with scabies.

2. Examination:
    a. Small papular rash with or without burrows in the webs of the fingers, wrists, the genitalia, the buttocks, the waist, the inner aspects of the thighs, and the axilla. The rash is generally bilaterally symmetrical.
    b. Excoriations may be present; some may be secondarily infected.

3. Laboratory:
    a. Although the mite can at times be extruded from a burrow, this requires a fair amount of experience and is not necessary to make a diagnosis. Scrape linear skin lesion with scapel with oil on it so skin scrapings stay on scapel. Roll onto slide - examine under low and high power look for mite, eggs or feces of mite. Hand lesions are more likely to be positive.

4. Diagnostic criteria:
    a. History of pruritic rash (itching wakes patient up at night).
    b. Characteristic rash (burrows in skin or characteristic pruritic, erythematous, papular eruptions), or common sites.
    c. Sexual exposure or close physical contact to a person infested with scabies mites.
    d. Exclusion of syphilis, if necessary.

B. Treatment

Recommended regimen: <u>Permethrin 5% cream</u> (Elimite cream or Acticin cream, 30 gram tube) applied from the neck down and washed off after 8-14 hours. It is not contraindicated in pregnancy or during lactation.

Crusted scabies

No controlled therapeutic studies for crusted scabies have been conducted, and the appropriate treatment remains unclear. Refer to CDC STD treatment guidelines. Oral ivermectin treatment is on the Public Health Formulary with ACD approval.

C. Follow-up

Symptoms or signs that persist for >2 weeks can be attributed to several factors. Treatment failure might be caused by resistance to medication or by faulty application of topical scabicides. Patients with crusted scabies might have poor penetration into thick scaly skin and harbor mites in these difficult-to-penetrate layers. Particular attention must be given to the fingernails of these patients. Reinfection from family members or fomites might occur in the absence of appropriate contact treatment and washing of bedding and clothing. Even when treatment is successful and reinfection is avoided, symptoms can persist or worsen as a result of allergic dermatitis. Finally, household mites can cause symptoms to persist as a result of crossreactivity between antigens. Some specialists recommend re-treatment after 1–2 weeks for patients who are still symptomatic; others recommend re-treatment only if live mites are observed. Patients who do not respond to the recommended treatment should be re-treated with an alternative regimen (see CDC guidelines for information on lindane and ivermectin).

D. Counseling/Education

Patients should:

1. Understand how to apply prescribed medication;
2. Trim fingernails closely to reduce injury from excessive scratching;
3. Return after two weeks for evaluation if symptoms persist (patients should be informed that the rash and pruritus may persist for up to 2 weeks after treatment);
4. Refer sex partner(s) for treatment; and
5. Avoid sexual or intimate contact until patient and partner(s) are treated.

E. Evaluation of Sex Partners

All sex partners, close personal or household contacts within the proceeding month should be promptly treated.

F. Special Considerations

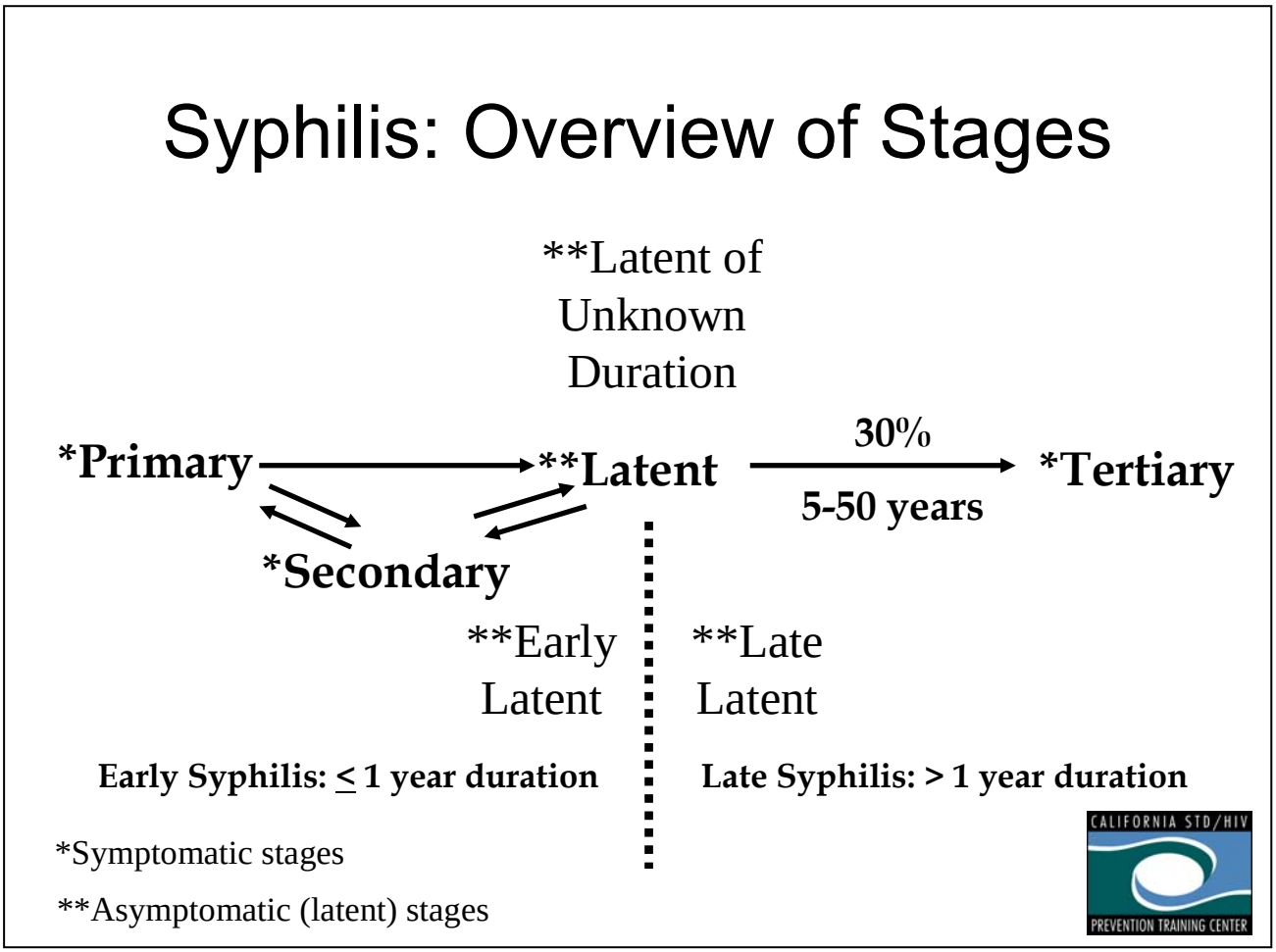
Decontamination of articles: clothing, bed linens, and towels that may have been used by the patient within the past one to two weeks should be washed and dried by machine (hot cycle in each) or dry cleaned. Articles that cannot be washed or dry-cleaned can be sealed in a plastic bag or placed in storage for 72 hours.

Syphilis

Syphilis is a sexually acquired infection caused by the spirochete, *Treponema pallidum*, which may become chronic without treatment. Transmission can occur horizontally through contact to moist mucosal lesions and vertically from mother-to-child during pregnancy. Syphilis is divided into four stages (primary, secondary, latent, and tertiary), which reflect the clinical progression of disease. Primary and secondary stages of syphilis reflect new or incident infections and are the infectious stages of syphilis, while other stages are considered prevalent infections. Primary and secondary stages primarily involve the skin and mucosal surfaces; latent disease has no clinical signs or symptoms; and late manifestations may affect virtually any organ system. Neurosyphilis can occur at any stage of the disease. Vertical transmission can also occur at any stage of syphilis.

Natural History and Clinical Manifestations

The natural course of untreated syphilis is depicted below:



Primary syphilis:

- Characterized by a painless ulcer (chancre) appears 10-90 days (average 21 days) after contact with an infected partner.
- Chancre is highly infectious and teeming with spirochetes. Usually heals spontaneously without scarring, in one to six weeks.
- While typical chancres are painless and singular, atypical lesions are fairly common. Patients could still have a primary lesion and report a painful sore or multiple sores. Multiple lesions occur in ~25% of patients and are more likely to occur in HIV positive patients.
- Patients may have minimally tender lymphadenopathy that usually occurs bilaterally.

Secondary syphilis:

- This stage can be characterized by the following:
  - **Skin rash** (~ 75-90% of patients) - May be generalized or localized at the genitals, ~60% involve the palms and soles. Usually non-pruritic.
  - **Generalized lymphadenopathy** (~70-90% of patients) - The enlarged lymph nodes are generally non-tender.
  - **Constitutional symptoms** (~50-80% of patients) – May include fever, headache, and/or malaise.
  - **Mucous patches** (~5-30% of patients) - Flat to slightly raised and usually painless patches found in the oropharynx or anogenital regions.
  - **Condyloma lata** (~5-25% of patients) - Moist wart-like papules and occur in warm, moist intertriginous areas such as the perineum and gluteal folds. These lesions are loaded with spirochetes and are highly contagious.
  - **Alopecia** (~10-15% of patients) – Patchy hair loss, resembling a moth eaten appearance, and most often occurs in the occipital and bitemporal regions. Hair loss can also occur on the eyelashes and the lateral third of the eyebrows.
- These signs and symptoms usually appear 3-6 weeks after the primary chancre appears. The primary chancre may also occur at the same time as the secondary manifestations in up to 1/3 of patients.
- Untreated secondary syphilis manifestations will resolve spontaneously after weeks to months.
- Relapses of secondary symptoms can occur (~25% of infected individuals), usually within the first year after infection.

Early Latent and Late Latent Syphilis

- Characterized by the absence of symptoms and signs.
- Categorized as **early** ≤ 1 year duration) or **late** (> 1 year duration).
- In order to be diagnosed as **early latent**, the patient must have had one of the following within the **past year:**
  - ✓ Documented seroconversion or fourfold or greater increase in titer of a non-treponemal test
  - ✓ Unequivocal symptoms of primary or secondary syphilis
  - ✓ A sex partner documented to have primary, secondary, or early latent syphilis
  - ✓ Reactive non-treponemal and treponemal tests when the only possible exposure occurred within the previous year.

Latent Syphilis of Unknown Duration

- For purposes of partner notification and **presumptive treatment** of exposed partners, there is another category called **latent syphilis of unknown duration.** This diagnosis is made in a patient who presents with:
  - ✓ No clinical symptoms and negative exam, and
  - ✓ No prior reactive serologic test for syphilis, and
  - ✓ Non-treponemal titer of 1:32 or greater and
  - ✓ Under 35 years old.
- These patients should receive treatment for late latent disease but are managed as cases of early latent disease in terms of partner notification procedures.

Tertiary syphilis:

- Since the widespread availability of antibiotics, tertiary syphilis is rarely diagnosed. If left untreated, ~30% of patients would progress to tertiary disease.
- Tertiary syphilis may include the following lesions:
  - o **Gummas** - granulomatous lesions likely formed as an immunologic response to treponemal antigens. These lesions destroy soft tissue, cartilage, and bone and can clinically mimic carcinoma. Gummas can also occur in mucosal areas and in viscera (lungs, stomach, liver, brain, genitals, eyes, and heart). Average onset of gummatous lesions is 10-15 years after initial infection.
  - o **Cardiovascular syphilis lesions** - endarteritis of the aortic vasovasorum and presents as ascending aortic aneurysm, aortic insufficiency, or coronary ostial stenosis. Average onset of cardiovascular syphilis is 20-30 years after initial infection.

- **Central nervous system (CNS) lesions** - include general paresis and/or tabes dorsalis. Patients may also present with dementia, psychosis, gait disturbances, lightning pains, or incontinence. Lesions of late neurosyphilis generally occur decades after initial infection.

Neurosyphilis:

- **Neurosyphilis can occur and be asymptomatic at any stage of disease**.
- Treponemal invasion of the CNS in early syphilis is fairly common, occurring in ~30-40% of patients and most of these patients will never have signs or symptoms and will clear the infection with benzathine penicillin G.
- Symptomatic early neurosyphilis usually occurs a few months to a few years after initial infection. Some evidence suggests that compared to HIV negative persons, HIV positive patients may be at increased risk for neurologic complications in early stages of syphilis.
- Most common manifestations of early neurosyphilis are:
  - **Acute syphilitic meningitis** - may present with typical meningitis symptoms such as headache, fever, photophobia, neck stiffness, nausea, and vomiting. Patients may also present with cranial nerve palsies, especially involving cranial nerves VI, VII, and VIII. Due to involvement of cranial nerve VIII, auditory complications including hearing loss are possible.
  - **Meningovascular syphilis** - an endarteritis that presents with seizures or as a stuttering stroke-like syndrome.
  - **Syphilitic eye disease** - manifestations may include uveitis, neuroretinitis, and optic neuritis. Ocular involvement can occur with both early and late stages of syphilis. The most common presentation in early syphilis is uveitis.
- Manifestations of late neurosyphilis are discussed above under tertiary syphilis section under "CNS lesions."

A. Diagnosis

1. History

a. General Considerations - Good sexual history with focus on the 5 "P's"

- **Partners**
  - Number and gender of partners will help determine patients at high risk for syphilis.
  - Exposure to known case of early syphilis (see Partner Management section for at-risk exposure periods based on stage of infection)
  - If no known infected contacts, inquire about signs and symptoms of syphilis in sex partners.

- **Practices**
  - Sexual practices (e.g. men reporting anal receptive intercourse) will help indicate patients at high risk for acquiring syphilis.
  - Also indicates possible sites of exposure (oral, anal, and/or vaginal) that would dictate where primary lesions are expected to occur.
- **Past STDs**
  - Patients with prior syphilis history may present with re-infection or treatment failure.
  - HIV-positive patients are more likely to acquire syphilis and to possibly have unusual manifestations.
  - Patients with other past STDs may be at greater risk of acquiring syphilis.
- **Prevention of STDs/HIV**
  - While condoms are not 100% protective, inconsistent or lack of condom use confer greater risk of acquiring syphilis.
- **Protection from pregnancy**
  - Risk of congenital syphilis must be considered in females who are at risk of becoming pregnant and are either infected with syphilis or exposed to a syphilis case.

b. **History and description of current infection** – onset, duration and location of symptoms and signs.

c. **Prior syphilis testing history**

- Look for prior negative tests if no history of previous syphilis infection.
- Look for previous titers if the patient has a past history of syphilis.

d. **History of conditions that could potentially cause biologically false positive syphilis serology -** such as acute viral illness, vaccinations, injection drug use, autoimmune or connective tissue disorders, and potential exposure to the other pathogenic treponemal infections; yaws, pinta, and bejel.

e. **History of current neurosyphilis symptoms:**

- Cognitive dysfunction
- Meninigitis symptoms (e.g., headache, nausea and vomiting, neck stiffness, fever, etc)
- Ophthalmic symptoms (e.g. blurry vision, photophobia, etc)
- Hearing loss
- Ataxia

2. **Physical Examination:**

a. Thorough examination of the oral cavity, lymph nodes, skin, palms and soles, genitalia, pelvic area, and perianal region should be done to look for signs of syphilis.

b. Neurologic examination should also be performed to assess for signs of neurosyphilis that include the following:

- Altered mental status
- Cranial nerve (CN) palsies involving CN VI, VII, and VIII
- Motor or sensory deficits
- Ophthalmic findings (e.g., uveitis, neuroretinitis, optic neuritis)
- Hearing loss (CN VIII)
- Signs of meningitis: Neck stiffness, fever, photophobia

3. Laboratory:

a. <u>Non-treponemal Tests:</u>

- **Non-treponemal** tests measure IgM and IgG antibody directed against a cardiolipin-lecithin-cholestrol antigen. They are not specific for *T. pallidum.*
- The most common non-treponemal tests are the microscopic **VDRL** (Venereal Disease Research Laboratory) and the macroscopic **RPR** (Rapid Plasma Reagin). **RPR is the non-treponemal test available in LA County clinics.**
- VDRL and RPR are not equivalent tests; patients with a prior syphilis history who have VDRL titers available cannot have these compared with RPR titers.
- Non-treponemal tests are used for:
  - Screening
  - Evaluation of patients with symptoms
  - Follow up assessment after treatment, can indicate treatment failure or re-infection
- The non-treponemal test is quantitative and the titers usually correlate with disease activity, making it a useful measure of response to therapy. A sustained (> 2 weeks) 4-fold change in titer, equivalent to a change of two dilutions (1:16 → 1:4 or 1:8 → 1:32) is considered necessary to demonstrate a clinically significant difference between two test results.
- Non-treponemal tests are usually 100% sensitive in secondary and latent syphilis.
- **Biologic false positive (BFP) non-treponemal tests -** Individuals with reactive non-treponemal tests and non-reactive confirmatory treponemal tests are called

BFP. A variety of conditions can cause false positive non-treponemal tests including:

- Viral illness
- Recent immunizations
- Injection drug use
- Autoimmune disorders
- Malignancy
- Aging
- Pregnancy.

Non-treponemal tests may also be positive with the other pathogenic treponemal diseases; yaws, pinta, or bejel.

- **Causes of false negative non-treponemal tests:**
  - **Early primary syphilis** - Can take up to 4 weeks from the initial appearance of the chancre before the non-treponemal test becomes positive. Up to 30% of early primary syphilis patients will have a non-reactive non-treponemal test at their initial visit. If suspicion is high for primary syphilis, ordering a treponemal test concurrently with a non-treponemal test (in patients without a history of prior syphilis) is useful as treponemal test often become positive before non-treponemal tests.
  - **Prozone phenomenon** – seen in early stages, usually in secondary syphilis. Prozone effect occurs when the concentration of antibody is high and the excess overwhelms the agglutination reaction. As the sample is diluted, agglutination occurs, resulting in a titer reading. If suspicion is high for secondary syphilis and the non-treponemal test is nonreactive, instruct the laboratory to dilute the serum to at least a 1/16 dilution to rule out the prozone effect.
  - **Late latent and tertiary stages** – sero-reversion of the non-treponemal test becomes more likely as the infection progresses to later stages. If there is a high index of suspicion for syphilis, a confirmatory treponemal test will confirm syphilis.

b. <u>Treponemal Tests:</u>

- Treponemal tests are specific for *T. pallidum* and measure antibody (IgM and IgG) directed against *T. pallidum* antigens by particle agglutination for the *Treponema pallidum* Particle Agglutination test **(TP-PA)** or by immunofluorescence for the Fluorescent Treponemal Antibody-Absorbed test **(FTA-ABS). TP-PA is the treponemal test available at LA County STD clinics.**

- The FTA-ABS test is a technically demanding test, and accuracy of results can vary due to reader dependency. When ordering an FTA-ABS from PHL, consultation with the LA County STD Program is required.
- Treponemal tests usually remain reactive for life, even after adequate treatment. However, 15-25% of patients who are treated during the primary stage of syphilis will sero-revert, usually after 2-3 years.
- Treponemal tests are used for:
    - Confirmation of positive non-treponemal tests
    - Screening the blood supply
    - Diagnosis of early primary and tertiary syphilis where the non-treponemal test may be falsely negative
    - Screening
    - Confirmation of reactive treponemal EIA/CIA with non-reactive RPR/VDRL results when treponema EIA/CIA tests are used as the initial screen.

- Treponemal tests are qualitative (not able to titer) and are not used to measure treatment response or to evaluate for possible treatment failure or re-infection.
- **False positive treponemal tests** – Occur rarely (< 1% of the general population) and can occur with collagen vascular diseases, mononucleosis, leprosy, Lyme disease, injection drug use, and aging. Treponemal tests will also be positive in the presence of the other pathogenic treponemal infections; yaws, pinta, and bejel.
- **False negative treponemal tests**:
    - While treponemal tests may turn positive before the non-treponemal tests during primary syphilis, they may still be negative in the very early stages of the disease. If primary syphilis is strongly suspected by history and physical but both non-treponemal and treponemal tests are initially nonreactive, repeat both tests again in one week and one month.
    - With prompt treatment in early syphilis, the non-treponemal test may never become reactive but the treponemal test will become reactive within one month, allowing for confirmation of the syphilis diagnosis.

Syphilis Testing Algorithms Using Treponemal Tests for Initial Screening[1,2]

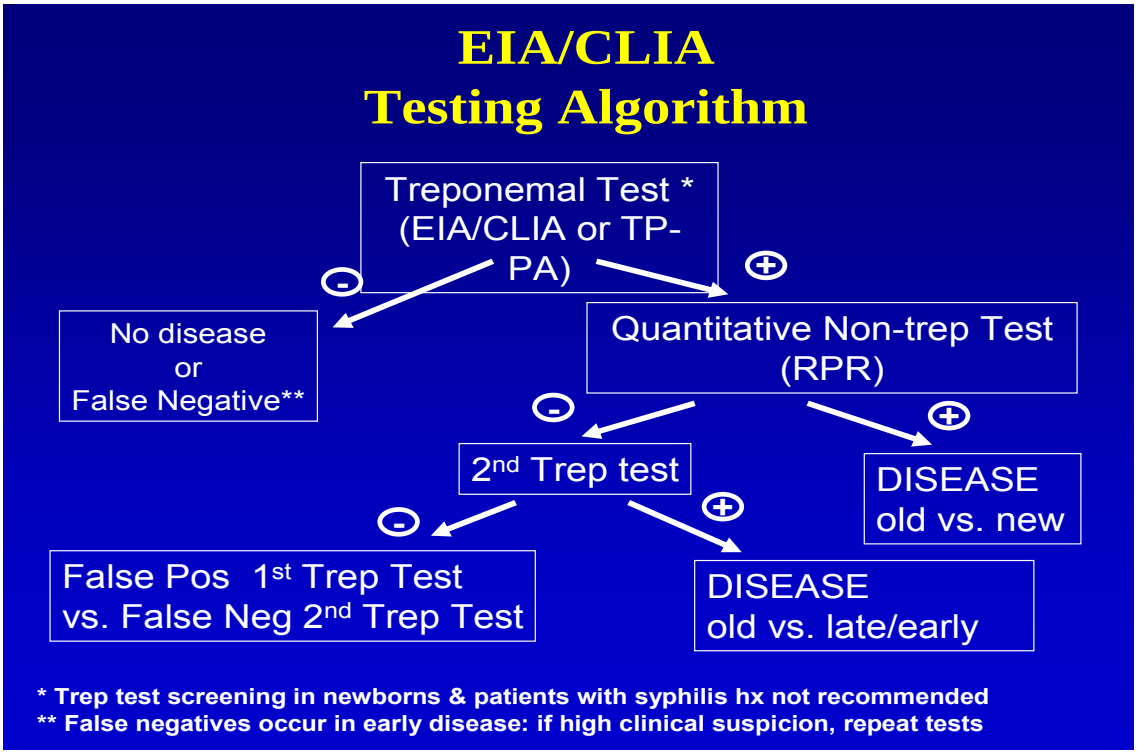
- Some high-volume clinical laboratories have begun using automated treponemal tests, such as automated enzyme immunoassays (EIAs) or

[1] CDC. Syphilis Testing Algorithms Using Treponemal Tests for Initial Screening---Four Laboratories, New York City, 2005—2006. *MMWR.* 2008;57(32):872-875.

[2] CDC. Discordant Results from Reverse Sequence Syphilis Screening – Five Laboratories, United States, 2006—2010. *MMWR.* 2011;60(05):133-137.

immunochemoluminescence tests (CLIAs), and have reversed the testing sequence: first screening with a treponemal test and then retesting reactive results with a nontreponemal test. This approach has introduced complexities in test interpretation that did not exist with the traditional sequence. Specifically, screening with a treponemal test sometimes identifies persons who are reactive to the treponemal test but nonreactive to the nontreponemal test.

- When results are reactive to both treponemal and non-treponemal tests, persons should be considered to have untreated syphilis unless it is ruled out by treatment history. Persons who were treated in the past are considered to have a new syphilis infection if quantitative testing on a treponemal test or another nontreponemal test reveals a four fold or greater increase in titer.
- When results are reactive to the treponemal test but nonreactive to the RPR test, persons with a history of previous treatment will require no further management.



- For persons without a history of treatment, a second, different treponemal test should be performed. If the second treponemal test is nonreactive, possible diagnoses are either: a false-positive initial treponemal test, very early untreated syphilis, or previously treated syphilis. Though most likely not syphilis, clinicians should consider the individual patient's risk for recent contact to infectious syphilis.
- If the second treponemal test is reactive, clinicians should discuss the possibility of infection and offer treatment to patients who have not been

previously treated. Unless history or results of a physical examination suggest a recent infection, such patients are unlikely to be infectious and should be treated for late latent infections, even though they do not meet the surveillance case definition. Treatment can prevent severe (i.e., tertiary) complications that can result from untreated syphilis, although the probability of such complications occurring without treatment, while unknown, likely is small. Treatment also allows patients to report that they have been treated for syphilis if they ever receive similar results from future treponemal screening tests. These are considered low priority for PHI intervention activities.

Serofast Status: A persistent, low-level positive non-treponemal titer (usually ≤ 1:8), suggesting a "serofast" state, has been found to occur in some patients. This phenomenon has been seen more often in HIV-coinfected individuals. This diagnosis is one of exclusion. Re-infection and treatment failure must be ruled out to determine an individual to be serofast.

Test sensitivity and serologic response by stage of infection:

Sensitivity of Serologic Tests According to Stage

Test	1°	2°	Latent	Tertiary
VDRL/RPR	74-87%	100%	88-100%	37-94%
FTA-ABS	70-100%	100%	100%	96%
MHA-TP*	69-90%	100%	97-100%	94%

*MHA-TP and TP-PA probably perform equivalently

Neurosyphilis diagnosis:

- Diagnosis depends on a combination of reactive serologic test results, abnormal CSF cell count and protein, and/or reactive VDRL-CSF, with or without clinical manifestations.
- In addition to abnormal CSF findings, patients with neurosyphilis must have clinical and/or laboratory evidence of *T. pallidum* infection (i.e. they meet the criteria for early or late disease).

Since neurologic involvement can occur at any stage of the disease, lumbar puncture (LP) should be done if there are symptoms or signs suggestive of CNS involvement (including ophthalmic or auditory symptoms), regardless of infection stage.

Indications for CSF exam[3] :

- **Primary, secondary, or early latent syphilis (≤ 1 year duration)**
  - Neurologic or ophthalmic/auditory symptoms or signs
  - Treatment failure

- **Late syphilis (> 1 year duration)**
  - Neurologic or ophthalmic/auditory symptoms or signs
  - Evidence of tertiary disease such as aortitis, gumma, or iritis
  - Treatment failure

Interpretation of CSF results:

- **VDRL-CSF** - standard test available and routinely performed on CSF specimens.
  - Low sensitivity, high specificity
    - False negative results are common
    - Nonreactive test does not exclude neurosyphilis diagnosis. Therefore, additional evaluation using FTA-ABS testing on the CSF can be considered. If both are nonreactive, neurosyphilis is highly unlikely.
    - False positive results are rare and are usually due to contamination of the CSF with blood.
    - A reactive test in the absence of gross blood contamination of the sample can be considered diagnostic of neurosyphilis infection.
- **CSF FTA-ABS** - *not available at PHL.*
  - High sensitivity, low specificity
    - False positive results common
    - Reactive test is not necessarily diagnostic of neurosyphilis
    - False negative results are rare and some specialists believe that a nonreactive test excludes the diagnosis of neurosyphilis.
- **CSF cell count and protein**
  - Are considered *abnormal* when:

[3] For instructions on the LP referral procedure, refer to LP Referral section of the manual.

- ✓ CSF WBC is > 5 WBC /mm^3 (In HIV infected patients, using a higher cut off of >20 WBC/mm^3 might improve the specificity of neurosyphilis diagnosis.).
- ✓ CSF protein is > 40 mg/dl.

o CSF cell count and protein tests have low sensitivity and low specificity.

o While abnormal results are not useful alone in making a neurosyphilis diagnosis, they can support the diagnosis when interpreted along with other test results and clinical findings.

o CSF WBC count can also be used to follow response to therapy.

- **<u>Darkfield Microscopy & Direct Fluorescent Antibody (DFA) Testing:</u>**

o *These tests are not currently available at LA County clinics.*

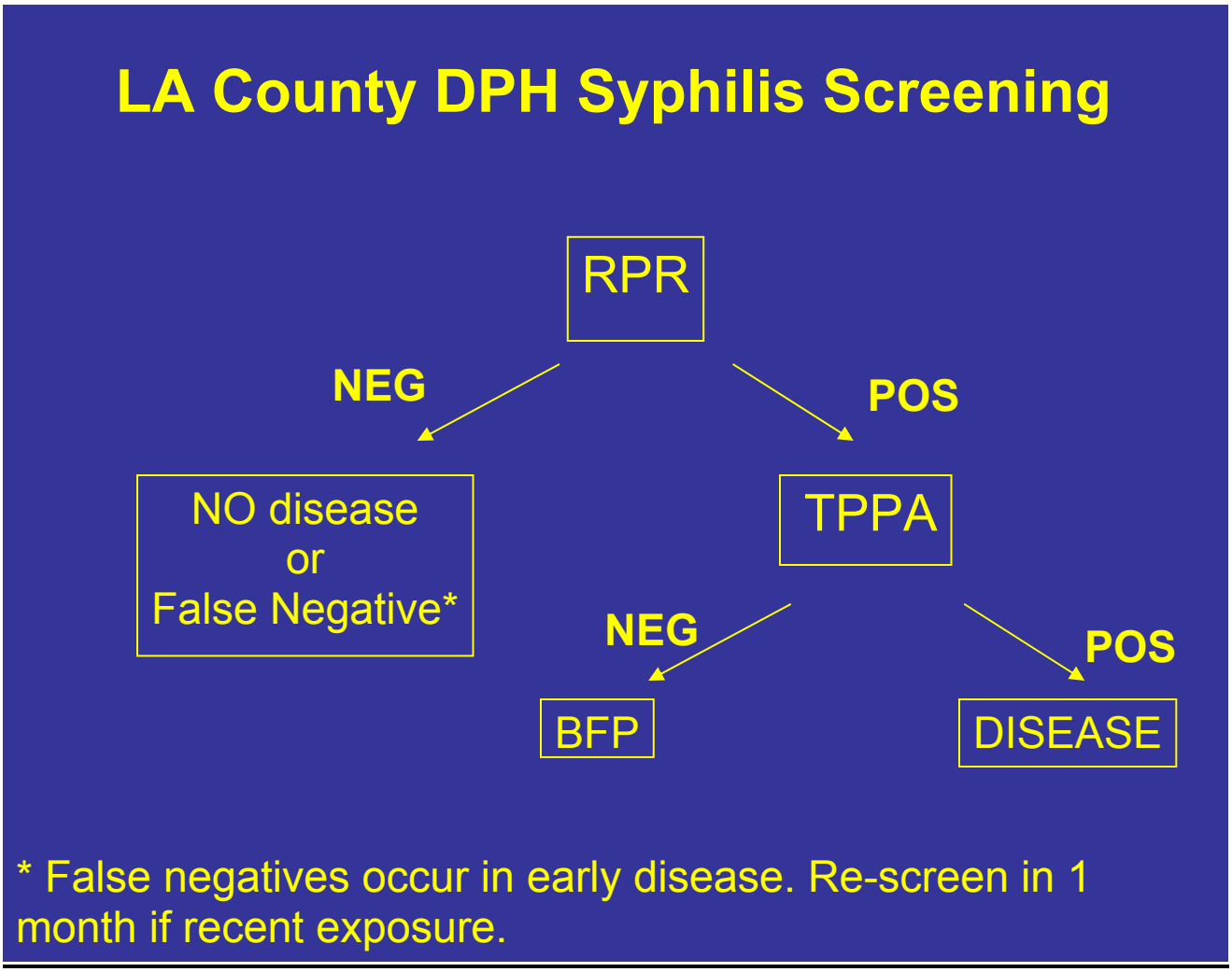
o Directly detect T. pallidum obtained from primary chancres or secondary mucocutaneous lesions.

o Spirochetes are more difficult to detect and tests may be falsely negative with older/drier lesions and with application of topical agents.

o Darkfield exam should not be performed on oral lesions. It can be falsely positive due to non-pathogenic treponemes found in the oral cavity. This does not occur with DFA testing and DFA can be performed on oral lesions.

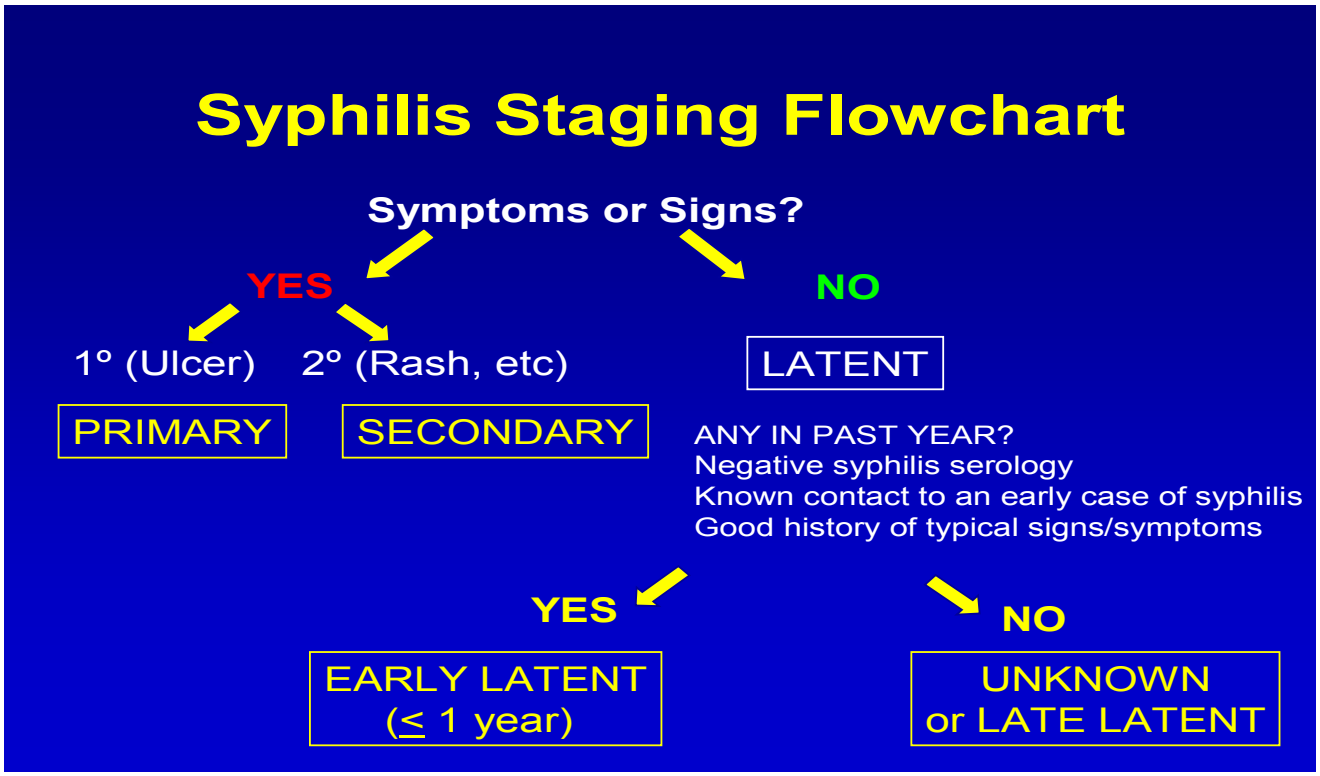
<u>LA County Clinic Syphilis Screening Algorithm:</u>

- All positive non-treponemal tests need to be confirmed with a treponemal test for initial diagnosis. At LA County clinics, an RPR is ordered at initial screening and if the RPR is reactive, the laboratory will <u>reflexively perform a TP-PA</u> as the confirmatory treponemal test.
- The screening algorithm for syphilis serology is as follows:



Note: This algorithm does not apply to sexual contacts exposed ≤ 90 days to early syphilis as RPR and/or TPPA may be falsely negative.

Syphilis staging: Syphilis staging is an important component of clinical diagnosis. Disease stage helps determine treatment and partner management. Below is a syphilis staging flowchart:


Syphilis Staging Flowchart
Symptoms or Signs?
YES
NO
1° (Ulcer)
2° (Rash, etc)
LATENT
PRIMARY
SECONDARY
ANY IN PAST YEAR?
Negative syphilis serology
Known contact to an early case of syphilis
Good history of typical signs/symptoms
YES
NO
EARLY LATENT
(≤ 1 year)
UNKNOWN
or LATE LATENT

B. Treatment

1. General Considerations:

- **Benzathine penicillin G (Bicillin LA) is the first-line treatment for non-neurosyphilis infection.** Avoid the inadvertent use of benzathine-procaine penicillin (Bicillin CR) as this is inappropriate therapy.
- Penicillin-allergic patients who are treated with a non-penicillin treatment should be cautioned regarding possible treatment failure and should be followed closely for serologic and symptomatic treatment failure.
- **Pregnant patients require penicillin therapy. No other treatment will suffice.** Pregnant women with a history of true penicillin allergy must be desensitized and treated with Bicillin LA (see Penicillin Desensitization Appendix).
- **Always draw an RPR titer on the day of treatment**, before beginning treatment. This will be the baseline for monitoring serologic response to therapy.
- All patients should be alerted to the possibility of a **Jarisch-Herxheimer reaction:**
  - Self-limited acute febrile reaction to anti-treponemal therapy that may be accompanied by chills, malaise, nausea/vomiting, headache, or myalgia.
  - An exacerbation of the secondary rash may occur.
  - More frequent with penicillin therapy and with treatment of early stages of syphilis, especially secondary.
  - Onset within 24 hours (usually 2-8 hours) after therapy; usually resolves within 24 hours.
  - Antipyretics may offer symptom relief but will not prevent the reaction from occurring.
  - Patients should be counseled that this is not an allergic reaction to penicillin.
  - Pregnant women should be informed that this reaction may be associated with early labor and/or fetal distress and be advised to go to the emergency room if contractions occur or if they notice decreased fetal movement.

2. Treatment of Primary, Secondary, and Early Latent Syphilis:

Antibiotic of choice:

Benzathine penicillin G 2.4 million units IM (administered as 1.2 million units IM in each buttock) **once.**

Alternative (for non-pregnant, penicillin-allergic patients):

- Doxycycline 100 mg orally BID for 14 days may be substituted (can also use tetracycline 500 mg PO QID for 14 days but more GI side effects and compliance is likely to be worse, compared to doxycycline).

- Some experts have also suggested using ceftriaxone 1 gm IM/IV QD for 8-10 days, although some patients who are allergic to penicillin will also be allergic to cephalosporins.
- Although azithromycin 2g once has shown efficacy, it should not be used in LA County STD Clinics due to antibiotic resistance seen in California.

2. Treatment of Late Syphilis, Latent Syphilis of Unknown Duration, and Tertiary Syphilis:

Antibiotic of choice:

- **Benzathine penicillin G 2.4 million units IM** (administered as 1.2 million units IM in each buttock) **once each week for three weeks**.
- Patients receiving three doses of penicillin must start their treatments over if more than 10-14 days has elapsed between doses. They should receive their bicillin no earlier than five days since the preceding dose.
- **Missed doses are not acceptable for pregnant women. If a dose is missed, then therapy must be restarted.**

***Alternative* (for non-pregnant, penicillin-allergic patients):**

- Doxycycline 100 mg orally BID for 28 days may be substituted (tetracycline 500 mg PO QID for 28 days can also be used but compliance is likely to be better with doxy).

3. Treatment of Neurosyphilis

Antibiotic of choice:

- Aqueous crystalline penicillin G 18-24 million units IV once daily, administered as 3-4 million units IV q 4 hours or as continuous infusion, for 10-14 days.

***Alternative*:**

- If IV treatment is not possible/desired and patient compliance can be assured, can use alternative treatment of procaine penicillin 2.4 million units IM (administered as 1.2 million units IM in each buttock) once daily plus probenecid 500 mg PO four times/day, both for 10-14 days.
- Non-pregnant penicillin allergic patients should ideally be desensitized and treated with penicillin. Some experts recommend an alternative treatment of ceftriaxone 2 gm IM/IV once daily for 10-14 days. However, some patients who are allergic to penicillin will also be allergic to cephalosporins. Efficacy data supporting this treatment is limited. If used, close follow-up is essential.
- For neurosyphilis in a patient with late latent syphilis or latent syphilis of unknown duration, benzathine penicillin G 2.4 million units IM (administered as 1.2 million units IM in each buttock) once each week for 3 weeks after completion of the neurosyphilis treatment is recommended in order to provide a total duration of therapy comparable to that used for late syphilis.

C. Follow-up

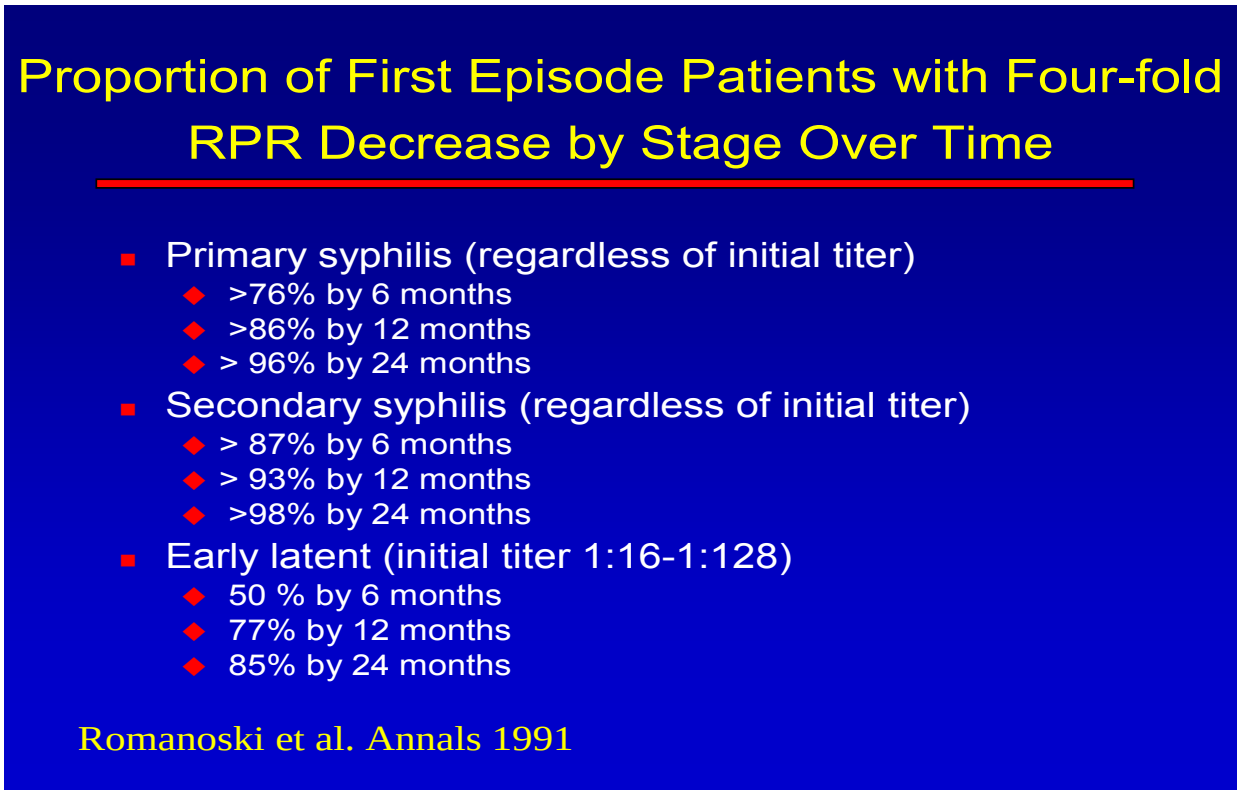
1. Primary and Secondary Syphilis

- **Clinical evaluation only** (no serology) – should be done at **1-2 weeks** and again at **1 month** after treatment.
  - Assess for improvement and resolution of symptoms.
  - Ask about any treatment complications**.**
  - Ask about any new neurological symptoms and refer to the emergency department for LP and treatment if they are present.
- **Serologic and clinical follow up** - should be done at **6 months** and **12 months** after therapy in non-HIV infected individuals.
  - Follow up RPR titers should be compared to the baseline titer obtained on the day of treatment.
  - Patients should also be assessed clinically for any new signs and symptoms of syphilis that might suggest re-infection or treatment failure as well as development of any neurological signs or symptoms.

2. Latent Syphilis

- **Clinical evaluation** – Early late latent patients should be seen 1-2 weeks after treatment. Late latent syphilis patients or those with syphilis of unknown duration should be seen by a clinician every week during the three weeks they are receiving penicillin therapy.
  - Assess for treatment complications.
  - Assess for the development of early syphilis and/or neurosyphilis signs or symptoms. If neurosyphilis signs or symptoms are present, refer to the emergency department for LP and treatment.
- **Serologic follow up** - should be done at **6, 12, and 24 months** after treatment in non-HIV infected individuals and titers compared to the baseline titer from the day of initial treatment.

3. Serologic Response to Therapy Over Time by Stage: The serologic response to appropriate treatment varies by stage. A four-fold decrease in titer is expected by 12 months in patients diagnosed with primary and secondary syphilis cases. A four-fold decrease in titers within 12-24 months is expected in patients with diagnosed with early latent syphilis and initial titers $\geq$1:16. Failure to drop by these time periods requires clinical consideration of treatment failure.



4. **<u>Treatment Failure or Re-Infection in Early and Late Syphilis</u>:**

- Patients should be **evaluated for treatment failure** if any of the following occur:
  - Clinical signs or symptoms persist or recur.
  - A sustained (> 2 weeks) 4-fold increase in titer occurs (using the same laboratory to evaluate titers for sustained rise is helpful).
  - <u>Primary and Secondary Syphilis</u>: Compared to baseline, titer fails to decline 4-fold within 6 -12 months.
  - <u>Latent syphilis</u>: Compared to baseline, an initially high (≥ 1:32) titer fails to decline 4-fold within 12-24 months.
- If evidence of treatment failure is present **and** low likelihood of re-infection:
  - For those without neurologic symptoms, refer for LP (See Referrals for Lumbar Puncture Appendix). For those with neurologic symptoms, refer to the emergency room for LP and treatment.
  - Repeat HIV test.
  - If CSF exam is abnormal, treat for neurosyphilis.
  - If CSF exam is normal, re-treat with benzathine penicillin G 2.4 million units IM (administered as 1.2 million units IM in each buttock) once each week for 3 weeks.

5. Neurosyphilis Follow-up

- Perform clinical and serological follow-up appropriate for the stage of syphilis.
- If CSF pleocytosis is present initially, the CSF exam should be repeated every 6 months until the cell count is normal. Re-treatment should be considered if CSF WBC count has not decreased after 6 months.
- Limited data suggest that in immunocompetent patients and HIV-infected on antiretroviral therapy, normalization of serum RPR predicts normalization of CSF parameters.
- Re-treatment should also be considered if CSF protein is not normal and/or VDRL-CSF is not negative after 2 years.

D. Special Considerations

1. HIV infection and syphilis:

- **HIV testing in syphilis patients** - **All cases of syphilis** should be tested for HIV. If the first HIV result is negative, patients with early syphilis should be retested for HIV in 3 months.
- **HIV co-infected syphilis cases are recommended to have a CSF exams when there is the following:**
  - Presence of neurologic symptoms, or
  - Evidence of treatment failure
- CSF exam is not needed in HIV positives diagnosed with syphilis and without neurologic symptoms or evidence of treatment failure. CSF abnormalities are common early in HIV-infected syphilis cases and the clinical and prognostic significance of CSF abnormalities in HIV-infected patients with early syphilis is unclear. In addition, CSF examination has not been associated with improved outcomes in this setting unless neurologic symptoms are present.
- For those diagnosed with neurosyphilis, follow-up CSF examination after treatment is essential.
- **Syphilis treatment in HIV-infected individuals:**
  - **Primary, secondary or early latent syphilis: benzathine penicillin G 2.4 million units IM** (administered as 1.2 million units IM in each buttock) **once.** Some experts recommend additional treatment once each week for three weeks, as recommended for late syphilis.
  - **Late latent or unknown duration syphilis: benzathine penicillin G 2.4 million units** (administered as 1.2 million units IM in each buttock) once each week for three weeks. Treatment should not be withheld while awaiting a screening LP. Benzathine penicillin G does not cross the blood-brain barrier well so starting treatment will not affect LP results.

- HIV-infected patients with penicillin allergy can be managed according to the recommendations for non-pregnant penicillin-allergic HIV-negative patients. Efficacy of alternative non-penicillin regimes in HIV-infected patients has not been well studied and as such, close serologic and clinical follow-up is required. HIV-infected penicillin-allergic patients whose compliance with therapy or follow up cannot be ensured should be desensitized and treated with penicillin.

- **Follow-up of HIV-infected individuals with syphilis:** As treatment failures occur more frequently, shorter follow-up for HIV-infected individuals is recommended to detect resisting titers.
  - For HIV-infected patients with **early** syphilis:
    - Repeat RPR titers should be done at **3, 6, 9, 12 and 24 months** after therapy.
    - Criteria for treatment failure/re-infection (See "Treatment Failure and Re-infection" section).
  - In HIV-infected individuals with **late** syphilis:
    - Repeat RPR titers should be done at **6, 12, 18, and 24 months after therapy**.
    - Criteria for treatment failure/re-infection (See Treatment Failure and Re-infection section).

2. **Pregnancy and syphilis:** Vertical transmission from mother-to-fetus caused by hematogenous spread may cause congenital syphilis, although direct contact with lesions at delivery may also lead to transmission to the infant. **Transmission to the fetus can occur at any stage of maternal infection with the risk of transmission significantly increased during incubating and early syphilis (~100%).**
   - **Syphilis screening:**
     - All pregnant women should be screened for syphilis at the first prenatal visit.
     - In areas of high syphilis prevalence, screening should be repeated in the third trimester between 28-32 weeks gestation, and again at delivery.
     - A urine pregnancy test should be performed on women at risk of becoming pregnant who are diagnosed with any stage of syphilis.
   - **Syphilis treatment and pregnancy:**
     - **Penicillin is the only therapy recommended for pregnant women. Pregnant women with penicillin allergy should be desensitized and treated with penicillin.**
     - For pregnant women with primary, secondary, or early latent syphilis, some experts recommend a second dose of benzathine penicillin G 2.4 million units

IM be administered 1 week after the initial dose. *This is not necessary in LAC clinics.*

- Pregnant women who are seropositive:
  - Should be considered infected and in need of treatment unless medical records clearly document both adequate treatment for stage, an appropriate decline in antibody titers, low and stable titers (RPR ≤1:4 and low risk for re-infection.
  - Pregnant women with documented appropriate therapy for stage, appropriate response, low and stable titers (RPR <1:4), and low risk for re-infection (monogamous, seronegative or treated partner, no high risk activities, or concurrent STDs) do not require therapy; however, if patients have higher titers or if there is any doubt about re-infection, then treatment should be considered.
  - Serofast pregnant women should have yearly titers on record. If there is a gap greater than 2 years in the serological record, a careful sexual history and partner syphilis risk should be evaluated to rule out possible re-infection.
- Women in the second half of pregnancy should be counseled about the risk of Jarisch-Herxheimer reaction during treatment and the possible subsequent risk of premature labor/fetal distress. These women should seek urgent medical attention if they experience contractions or decreased fetal movement right after treatment. While stillbirth is a rare complication of the Jarisch-Herxheimer reaction, concern over this complication should not delay treatment.

- **Follow-up of pregnant women with syphilis:**
  - Pregnant patients diagnosed with syphilis should have repeat serology **as recommended for their stage of infection,** along with a titer in the **third trimester (28-32 weeks gestation) and again at delivery.**
  - Serofast untreated women should have an RPR drawn in the third trimester and at delivery.
  - Women at high risk of re-infection or who are poorly compliant with follow-up should be **evaluated and have an RPR drawn monthly.**
  - Clinical and serologic response post therapy should be **appropriate for the stage of infection**.
    - For those with primary and secondary syphilis, response should reflect a four-fold or greater decline in nontreponemal titer by 6-12 months.
    - For those with latent syphilis and initial titer ≥1:32, response should reflect a four-fold or greater decline by 12-24 months.
    - The majority of pregnant women will deliver before their serologic response to treatment can be assessed definitively.

- Inadequate maternal treatment and subsequent **need for infant treatment** is likely if:
  - Delivery occurs within 30 days of completion of therapy.
  - Clinical signs of infection are present in the woman at the time of delivery.
  - The maternal antibody titer at delivery is 4-fold higher than her pre-treatment titer.

E. Partner Management

- Sexual transmission of syphilis occurs only when mucocutaneous lesions are present. This is rare after the first year of infection. However, all sex partners of patients with syphilis in any stage should be evaluated clinically and serologically.
- A sex partner is considered at-risk for developing syphilis if their sexual exposure to the infected patient occurred within the following time periods:
  - **3 months** plus duration of symptoms for a patient with **primary** syphilis
  - **6 months** plus duration of symptoms for a patient with **secondary** syphilis
  - **1 year** for a patient with **early latent** syphilis.
- Partners who were **exposed ≤ 90 days** preceding the diagnosis of primary, secondary, or early latent syphilis in the index patient may be infected **even if seronegative**; therefore, these partners should be **treated presumptively**..
- Partners who were exposed > 90 days before the diagnosis of primary, secondary, or early latent syphilis in the index patient should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- For purposes of partner notification and presumptive treatment of exposed partners, patients with late latent and latent syphilis of unknown duration who have high nontreponemal titers (i.e., ≥ 1:32) should be assumed to have early syphilis and treated presumptively.
- Long-term sex partners of patients with late syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation findings. **Asymptomatic contacts of late syphilis do not need further testing if their non-treponemal serology is nonreactive.**
- Contacts should be treated with benzathine penicillin G unless there is a medical contraindication.

F. Counseling/Education

1. Syphilis cases should:

- Be referred to a PHI (Public Health Investigator) for counseling and partner/cluster elicitation.
- Understand the importance of returning for follow-up treatment.
- Be aware that the Jarisch-Herxheimer reaction may occur with treatment.
- Return for follow-up serologic tests as indicated.
- Refer sex partners(s) for examination and treatment.
- Avoid sexual activity until partner(s) are treated.
- Avoid sexual activity until one week after their treatment is completed.
- Use condoms to prevent future infections.
- Understand that syphilis has been associated with an increased risk of HIV transmission and that all syphilis patients should be HIV tested.

2. Syphilis partners/clusters should:

- Be aware that the Jarisch-Herxheimer reaction may occur.
- Avoid sexual activity until one week after treatment.
- Use condoms to prevent future infections.
- Understand that syphilis has been associated with an increased risk of HIV transmission and that all syphilis patients and their contacts should be HIV tested.

H. Reporting

- Submit CMR within <u>one working day</u> to the STD Program.
- Reporting should not be delayed until therapy can be recorded. A CMR should be submitted at the time of diagnosis and if necessary, updated when all doses of therapy have been completed.
- For congenital syphilis, separate CMR forms are required for mother and baby.

Appendices (on STD Program intranet page)

- Presumptive Treatment of Sex Partners of syphilis Cases - MEMO
- Referral for Lumbar Puncture (LP)
- Penicillin Desensitization
- Syphilis Record Card (H-3037) FAQs and Examples
- Evaluating for Primary Syphilis (California STD/HIV Prevention Training Center, 2003)
- Evaluating for Secondary Syphilis (California STD/HIV Prevention Training Center, 2003)

Trichomoniasis

Trichomoniasis is a sexually transmitted infection caused by the single-celled protozoan parasite Trichomonas vaginalis. Female patients may be asymptomatic, or they may present with itching and malodorous vaginal discharge. Male sex partners are usually asymptomatic, but urethritis may develop. There is a strong association with other STDs, particularly gonorrhea, so STD screening is indicated. There may be an association between trichomoniasis and adverse pregnancy outcomes, particularly premature rupture of the membranes and preterm delivery, however metronidazole treatment has not been shown to reduce perinatal morbidity. There is increasing evidence for epidemiologic and biologic interaction between HIV and T. vaginalis. T. vaginalis infection in HIV-infected women might enhance HIV transmission by increasing genital shedding of the virus, and treatment for T. vaginalis has been shown to reduce HIV shedding.

A. Diagnosis

1. History:
    a. Patients may be asymptomatic.
    b. If symptomatic, women typically present with a malodorous vaginal discharge and vaginal itching. Dysuria may be present.
    c. Men may present with dysuria or penile discomfort.

2. Examination:
    a. Profuse, malodorous frothy, gray, yellow or greenish discharge is typical although, the discharge may be scant and thin and white.
    b. Vaginal and cervical erythema may be present and the cervix may have punctate hemorrhages (strawberry cervix).

3. Laboratory:
    a. Vaginal pH >4.5 or normal.
    b. Whiff test positive or negative.
    c. Identification of motile trichomonads on a wet mount saline preparation (note that trichomonads die quickly so the saline preparation should be evaluated immediately after the pelvic exam has been completed). There will also be many white cells so close examination is necessary. Screen on low power for movement of organism.
    d. Culture and other more sensitive tests for trichomonas are not currently available in the STD clinics.

4. Diagnostic criteria:
    a. Identification of the motile T. vaginalis organism (that has a characteristic undulating membrane and flagella) by microscopic examination of a wet mount of vaginal discharge, urethral discharge, urine sediment or pap smear. The white blood cell count may be raised with a PMN:EC ratio>1 and >5 wbc/hpf.

b. The wet mount is insensitive in men and in women the sensitivity is approximately 60-70%. Therefore, the diagnosis may have to be made on clinical grounds alone.
c. While the sensitivity of a Pap test for T. vaginalis diagnosis is poor, use of a liquid-based testing has demonstrated enhanced sensitivity; however, false-positive tests can occur, and confirmatory testing might be needed in some circumstances.

B. Treatment

1. Primary

Recommended regimen:
Metronidazole 2 grams PO once.

Note: Tinidazole 2 g PO once is also recommended by the CDC but it is costly and is not on the PH formulary for routine trichomonas treatment.

Alternative Regimen:
Metronidazole 500 mg orally twice a day for 7 days

2. Recurrence and treatment failure

Rarely, resistance of trichomoniasis to metronidazole occurs. In evaluating a female or male patient for possible metronidazole resistant trichomoniasis obtain a careful history to assess for re-infection or new infection.

Some strains of *T. vaginalis* can have diminished susceptibility to metronidazole; however, infections caused by the majority of these organisms respond to tinidazole or higher doses of metronidazole. Low-level metronidazole resistance has been identified in 2%–5% of cases of vaginal trichomoniasis. High-level resistance is rare. Tinidazole has a longer serum half-life and reaches higher levels in genitourinary tissues than metronidazole. In addition, many *T. vaginalis* isolates have lower minimum inhibitory concentrations (MICs) to tinidazole than metronidazole.

a. If re-infection is likely, retreat with **Metronidazole** 2 grams PO once.

b. If re-infection is excluded or patient fails to respond to metronidazole 2 g single dose, the patient can be treated with **Metronidazole** 500 mg PO BID for seven days.

c. Patients who fail either of these regimens, treat with **Metronidazole** 2 grams PO qd for five days. An alternative, for patients who cannot tolerate metronidazole, is tinidazole 2 g orally for 5 days.

d. If these therapies are not effective, further management should be discussed with the STD Program. Consultation and *T. vaginalis* susceptibility testing to metronidazole and tinidazole is available from CDC (telephone: 404 718 4141; http://www.cdc.gov/std).

Metronidazole and tinidazole are both nitroimidazoles. Topical therapy with drugs other than nitroimidazoles can be attempted, but cure rates are low (<50%).

C. Follow-up

Routine follow-up is not required for men and women who become asymptomatic after treatment or who are initially asymptomatic.

D. Counseling/Education

Patients should:

1. Be counseled about the sexual transmission of trichomoniasis.
2. Patients should be advised to avoid consuming alcohol during treatment with metronidazole or tinidazole. Abstinence from alcohol use should continue for 24 hours after completion of metronidazole or 72 hours after completion of tinidazole.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination for other STD and treatment.
5. Avoid sex for at least 7 days after patient AND partner(s) are treated and symptom free.
6. Use condoms to prevent future infections.
7. Know that males frequently are asymptomatic even if infected.
8. Know that trichomoniasis, like other STDs, increases the risk of HIV transmission.
9. Re-screen women with HIV infection 3 months after treatment (see HIV below).

E. Evaluation of Sex Partners

Partners should present for STD screening and presumptive treatment (using therapy as for B.1. primary).

Although no data are available to guide treatment of the male partners of women with nitroimidazole treatment failure, on the basis of expert opinion, male partners should be evaluated and treated with either tinidazole in a single dose of 2 g orally or metronidazole twice a day at 500 mg orally for 7 days.

Special Considerations

Allergy, Intolerance, and Adverse Reactions

Metronidazole and tinidazole are both nitroimidazoles. Patients with an immediate-type allergy to a nitroimidazole can be managed by metronidazole desensitization in

consultation with a specialist. Topical therapy with drugs other than nitroimidazoles can be attempted, but cure rates are low (<50%).

Pregnancy

All symptomatic pregnant women should be treated. Women can be treated with 2g metronidazole in a single dose at any stage of pregnancy.

Recommended regimen:

Metronidazole 2 grams PO once.

Note: The safety of tinidazole in pregnant women, however, has not been well evaluated. Choice of tinidazole in pregnancy should be deferred to OB-GYN.

Asymptomatic pregnant women with trichomoniasis should be counseled regarding their treatment options which include prompt treatment of the STI or deferral of treatment until after 37 weeks gestation.

Vaginal trichomoniasis has been associated with adverse pregnancy outcomes but metronidazole treatment has not been shown to reduce peri-natal morbidity. Although some trials suggest the possibility of increased prematurity or low birth weight after metronidazole treatment, limitations of the studies prevent definitive conclusions regarding risks for treatment. Treatment of T. vaginalis might relieve symptoms of vaginal discharge in pregnant women and might prevent respiratory or genital infection of the newborn and further sexual transmission.

Lactation

Lactating women treated with metronidazole should be advised that withholding breastfeeding during treatment and for 12–24 hours after the last dose will reduce the infant's exposure. For women treated with tinidazole, interruption of breastfeeding is recommended during treatment and for 3 days after the last dose.

HIV Infection

HIV-positive women who are sexually active should be screened for trichomoniasis at entry into HIV care, annually, and 3 months after treatment for trichomonas.

There is recent evidence to suggest Metronidazole 500 mg orally twice a day for 7 days is more effective than metronidazole 2 gm orally in a single dose.

Warts

Genital warts, or *condyloma acuminata*, are caused by many subtypes of human papillomavirus (HPV), small DNA viruses. Genital warts are usually flat, papular, or pedunculated growths on genital mucosa. Patients who develop warts due to HPV may have single or multiple soft, fleshy, growths anywhere around the anogenital region, which can be painless, painful, friable, or puritic depending on the lesion size and/or location. External genital warts are warts found on external genitalia: penis, vulva, scrotum, perineum, and perianal skin. Genital warts can occur on the cervix, in the vagina, urethra, and anus. The majority of external genital warts are caused by HPV types 6 and 11. Asymptomatic genital HPV infection occurs more frequently than visible genital warts. Patients with altered/impaired immune function (e.g. pregnancy, HIV) are more likely to have extensive or recurrent warts.

The differential diagnosis of external genital warts includes several acquired conditions as well as variations of normal anatomy. Acquired conditions include condyloma lata (the flat warts of secondary syphilis), molluscum contagiosum, lichen planus, melanocytic nevi, and seborrheic keratosis. Normal anatomic variations that may mimic warts include pearly penile papules, Tyson's glands, micropapillomatosis labalis, skin tags, and sebaceous glands.

A. Diagnosis

1. History:
    a. Most common complaint is cosmetic appearance of the wart without other physical symptoms, however itching is not uncommon.
    b. Known exposure to genital warts is infrequent.

2. Examination:
    a. Bright light with or without magnification should be used.
    b. Warts have a characteristic fleshy appearance, can be flat, papular, or pedunculated, and range in size between 1-5 mm. Warts that have been present for a long time may be larger and keratotic. Grouped warts may attain a size of several centimeters.

3. Laboratory:
    a. All patients with an initial diagnosis of genital warts must have an RPR done to rule out condyloma lata.
    b. Patients with extensive or refractory warts should have HIV infection ruled out.

c. Lesions that are pigmented, indurated, fixed, bleeding, or ulcerated should be biopsied to rule out neoplasia. Biopsy is also indicated if the diagnosis is uncertain or if lesions do not respond or get worse during treatment, especially if the patient is immunocompromised.

d. HPV DNA testing is not indicated in the diagnosis and management of genital warts.

e. Cervical colposcopy is indicated in the management of cervical warts and in the follow up of many abnormal Pap lesions. Outside of these conditions, colposcopy is not indicated in the management of females with genital warts.

4. Diagnostic criteria:

   a. Appearance of typical condyloma on visual inspection alone.

B. Counseling/Education

The following key counseling messages should be conveyed to all patients diagnosed with HPV infection:

- Genital HPV infection is very common. Many types of HPV are passed on through genital contact, most often during vaginal and anal sexual contact. HPV can also be spread by oral sexual contact.
- Most sexually active adults will get HPV at some point in their lives, though most will never know it because HPV infection usually has no signs or symptoms.
- In most cases, HPV infection clears spontaneously, without causing any health problems. Nevertheless, some infections do progress to genital warts, precancers, and cancers.
- The types of HPV that cause genital warts are different from the types that can cause anogenital cancers.
- Within an ongoing sexual relationship, both partners are usually infected at the time one person is diagnosed with HPV infection, even though signs of infection might not be apparent.
- A diagnosis of HPV in one sex partner is not indicative of sexual infidelity in the other partner.
- Treatments are available for the conditions caused by HPV (e.g., genital warts), but not for the virus itself.
- HPV does not affect a woman's fertility or ability to carry a pregnancy to term.
- Correct and consistent male condom use might lower the chances of giving or getting genital HPV, but such use is not fully protective, because HPV can infect areas that are not covered by a condom.
- Sexually active persons can lower their chances of getting HPV by limiting their number of partners. However, HPV is common and often goes unrecognized; persons with only one lifetime sex partner can have the infection. Two HPV vaccines are available, both of which offer protection against the HPV types that

cause 70% of cervical cancers (i.e., types 16 and 18); the quadrivalent vaccine (Gardasil) also protects against the types that cause 90% of genital warts (i.e., types 6 and 11). These vaccines are most effective when all doses are administered before sexual contact. Either vaccine is recommended for 11- and 12-year-old girls and for females aged 13–26 years who did not receive or complete the vaccine series when they were younger. The quadrivalent HPV vaccine can be used in males aged 9–26 years to prevent genital warts.

Additionally, the following are specific counseling messages for those persons diagnosed with genital warts and their partners:

- It is difficult to determine how or when a person became infected with HPV; genital warts can be transmitted to others even when no visible signs of warts are present, even after warts are treated.
- Genital warts are not life threatening. If left untreated, genital warts might go away, stay the same, or grow in size or number. Except in very rare and unusual cases, genital warts will not turn into cancer.
- Genital warts commonly recur after treatment, especially in the first 3 months.
- It is not known how long a person remains contagious after warts are treated.
- While treatment may induce wart free periods, it may not change the duration of infectivity or the risk of HPV transmission to sex partners.
- The primary goal of treatment is the cosmetic removal of visible warts and to alleviate any symptomatic warts. Since treatment can also have associated adverse effects and complications, care must be taken that the risks do not outweigh the benefits.
- Women should get regular Pap tests as recommended, regardless of vaccination or genital wart history. Women with genital warts do not need to get Pap tests more often than recommended.
- Correct and consistent male condom use can lower the chances of giving or getting genital warts, but such use is not fully protective because HPV can infect areas that are not covered by a condom.

C. Treatment

General Considerations:

Warts are treated for cosmetic purposes and symptom management. There are no medical indications for treating asymptomatic warts. Left untreated, visible warts might resolve, remain unchanged, or increase in size or number. Eventually, most patients will have spontaneous clearance (if immunocompetent). There is no evidence that wart treatment decreases transmission.

Patients should be warned that complications are rare but can include hypo or hyperpigmentation, depressed or hypertrophic scarring, and hyperesthesia at the treatment site.

There is no evidence that any specific treatment is superior to any of the others. Consideration in the choice of therapy includes provider experience, patient preference, side effects, and costs.

Recommended Regimens for External Genital Warts

Provider-Administered Therapies:

1. **Liquid nitrogen (LN2)**

Apply topically with a swab. The swab should be left on the wart(s) for approximately 10 seconds, the wart should be allowed to thaw, and then the treatment should be repeated. Large warts may be treated multiple times in one session. When available, a "cryo-gun" applicator may be used in place of cotton swabs, this is particularly convenient when faced with large lesions. Pain after application, followed by necrosis and sometimes blistering, is common. This treatment can be repeated every one to two weeks, as necessary. LN2 is considered safe for use in pregnancy. LN2 can also be used for urethral meatus warts.

2. **Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90% in alcohol:**

A small amount should be applied with a cotton swab or the broken end of a wooden swab in a thin layer so that a white "frosting" develops. Extreme care must be used when applying it to prevent burns to normal surrounding skin. It should be applied sparingly and allowed to dry before the patient sits or stands. Excess unreacted acid on normal skin can be neutralized with talc, sodium bicarbonate (baking soda), or liquid soap. This treatment is useful for warts on mucous membranes. It can be repeated weekly, if necessary. TCA and BCA are considered safe for use in pregnancy.

Note: Podophyllin resin is no longer available in the CHS STD clinics.

Patient-Applied Therapies

The best candidates for patient-applied treatments are those that can understand and comply with the treatments and those that can identify and reach all genital warts that need to be treated. Patients also need to have easy access to soap and water. If there is any concern that the patient does not understand the instructions or will not be able to apply the treatment correctly, then a provider applied treatment modality should be used instead. The provider should apply the initial treatment to demonstrate proper application technique and to identify the warts that need to be treated.

These treatments are not for use in pregnancy.

1. **Podofilox 0.5% solution (3.5 ml) or gel (3.5g)**

This treatment is applied with a cotton swab or finger (with gel only) to visible wart(s) BID for three consecutive days followed by four days without treatment. This cycle can be repeated as necessary up to a total of four times. Many patients will experience mild to moderate pain or local irritation after treatment. The total wart area treated should not exceed 10 cm^2 per day and the total volume of podofilox should be limited to 0.5 ml per day. This treatment is not safe for use in pregnancy.

2. **Imiquimod 5% cream (12 packets)**

This treatment is applied with a fingertip at bedtime three times a week for as long as sixteen weeks. It should be washed off with a mild soap and water 6-10 hours later. Mild to moderate local redness and irritation are common with this treatment and hyperpigmentation and hypopigmentation have been described. This treatment is not safe for use in pregnancy.

Note: Sinecatechins 15% ointment, a green tea extract, is now a CDC recommended patient applied treatment but is not on the PH formulary. It has to be applied 3 times a day, weakens condoms and is not recommended for people with HIV or other immunosuppressive disease, genital herpes or pregnancy.

D. Follow-up

Patients being treated with LN2, TCA, and podophyllin should return at 1-2 week intervals for re-treatment until lesions have disappeared and the skin is healed. Scabbed lesions are not suitable for treatment. Patients being treated with imiquimod or podofilox should follow-up for severe side effects or treatment failure.

If warts are persistent after 3 months, or poor response to treatment, consider biopsy to exclude a premalignant or neoplastic condition, especially in an immunocompromised person.

E. Evaluation of Sex Partners

Sex partner evaluation is of no proven benefit in preventing transmission, re-infection, or complications. Evaluation of partners does provide an opportunity to perform other STD screening. HPV testing is not indicated for partners of persons with genital warts.

F. Special Considerations

1**. Pregnancy:**
During pregnancy, genital warts often appear for the first time, or if already present, they may proliferate and become friable. They often resolve spontaneously postpartum.

Podophyllin, podofilox, and imiquimod are not approved for use during pregnancy.

Genital warts may be transmitted to infants during delivery and in extremely rare cases this can cause recurrent respiratory papillomatosis (wart-like growths on the larynx). Since the risk of developing RRP is thought to be quite low and it is unclear if cesarean delivery can prevent it, cesarean delivery of pregnant women with warts is not indicated if performed solely to prevent transmission of HPV to the newborn. Cesarean delivery may be indicated if a woman has numerous genital warts that obstruct the pelvic outlet or friable warts that might result in excessive bleeding during vaginal delivery.

2. HIV Infection:

There is currently no evidence to suggest that different treatment modalities should be used in HIV positive and HIV negative persons. However, HIV infected patients with genital warts may have larger or more numerous warts, may not respond to therapy as well as HIV negative persons, and may have more frequent recurrences post treatment.

The risk of progression to squamous cell carcinoma may also be greater in HIV infected patients and any atypical lesions should be promptly referred for biopsy.

G. Referral:

Referral should be made for biopsy of warts that are atypical or hyperpigmented. Referral for surgical removal should be considered for warts that cover an unusually large area or do not respond to treatment.

Referral should also be made for warts in the vagina, on the cervix, or anal mucosa. Distal urethral meatus warts may be treated in clinic, all other urethral warts should be referred to urology for treatment.

Referrals should be made to the appropriate specialty clinic at the nearest Comprehensive Health Center or County Hospital facility. If there is difficulty referring to your clinic's nearest facility, referrals can be made to LAC-USC or Harbor-UCLA Hospitals.

Appendices (on STD Program intranet page)

- Dear colleague letter on HPV testing and cervical cancer screening
- HPV Basics B-521 Brochure (English)
- HPV Basics B-521S Brochure (Spanish)

STDs by Syndrome

Cervicitis

Cervicitis is a clinical syndrome characterized by a purulent or mucopurulent cervical exudate and/or endocervical friability. Patients are frequently asymptomatic but may present with complaints of discharge, intermenstrual/coital bleeding or dysparunia. Chlamydia trachomatis or Neisseria gonorrhoeae are the most common pathogens associated with cervicitis, but in most cases no etiologic organism can be identified. Herpes simplex virus, and Trichomonas vaginalis can also produce cervicitis. Bacterial vaginosis and Mycoplasma genitalium have also been associated with cervicitis. Non-infectious causes of cervicitis include douching and other exposure to irritants, persistant abnormalities of vaginal flora, and idiopathic inflammation of the zone of ectopy.

A. Diagnosis

1. History:
   a. Cervicitis is frequently asymptomatic.
   b. If symptomatic, patient may complain of vaginal discharge, coital bleeding, pain with intercourse, pain with urination, or intermenstrual bleeding.
   c. The patient may have a partner who was diagnosed with urethritis.
   d. The patient may report douching.

2. Examination:
   a. Purulent or mucopurulent cervical exudate visible in os.
   b. Pus or mucopus apparent on first cotton swab inserted in os (positive swab test). It is often helpful to hold the swab against a white paper background for contrast. Note sustained endocervical bleeding after swab test.
   c. Bimanual exam to assess PID.

3. Diagnostic criteria for cervicitis: (requires a and/or b)
   a. Purulent or mucopurulent cervical exudate visible in os or on swab test, AND/OR
   b. The demonstration of sustained endocervical bleeding when the first swab is placed in the endocervix, also known as friability (note: bleeding from a cytobrush is not friability).

   In addition, the absence of an inflammatory vaginitis (i.e. no yeast or trichomonas seen), finding the vaginal fluid with >10 WBC per HPF is a sensitive predictor of cervicitis caused by chlamydia and/or gonorrhea.

4. Laboratory:
    a. Wet mount for diagnosis of vaginitis pathogens and leukorrhea.
    b. Nucleic acid amplification (NAAT) test for chlamydia and gonorrhea.
    c. Cervical specimen for HSV PCR.
    d. If wet mount negative for trichomonas, collect specimen for trichomonas culture or PCR (if available).

B. Treatment

As cervicitis is often not caused by chlamydia and gonorrhea, several factors should affect the decision to provide presumptive therapy for chlamydia and/or gonorrhea or to await the results of diagnostic tests: the patient's risk factors for CT/GC infection, whether NAAT tests are being used (always in LAC STD clinics), and the likelihood of follow-up for treatment based on laboratory findings.

- Treat presumptively for CT if :
    - ≤25, new or multiple sex partners, or recent CT infection
- Treat presumptively for CT and GC if:
    - Prevalence of GC is high (>5%) among women in clinical setting.
    - Patient at high risk/risk group for gonorrhea (previous gonorrhea infection, African-American)
    - Follow-up unlikely
- No presumptive treatment is necessary if patient is low risk for CT/GC and follow-up is likely.

Treatment for trichomonas or symptomatic bacterial vaginosis should be provided if diagnosed by microscopy.

C. Follow-up

1. If symptoms persist, women should be instructed to return immediately for re-evaluation.
2. Patients diagnosed with chlamydia or gonorrhea should return in 3 months for repeat testing.

D. Counseling/Education

Patients should:

1. Receive explanation about possible causes for cervicitis and routes of transmission.
2. Be counseled about the potential health consequences of untreated cervicitis caused by an STD.
3. If indicated, understand how to take prescribed oral medications and abstain from sex for at least 7 days and until sex partners have been treated.
4. Return for evaluation if symptoms persist.
5. Condoms are protective against STDs associated with cervicitis.
6. Explain the need for referral of all sex partners from past 60 days.

E. Evaluation of Sex Partners

Men who are sex partners in the past 60 days of women with cervicitis should be examined for STDs and treated with the same regimen that the index patient received.

F. Recurrent and Persistent Cervicitis

1. Evaluate for treatment non-compliance and re-exposure to an STD.
2. Re-assess vaginal flora. Treat any vaginal infections (including asymptomatic BV). Consider treating for trichomonas.
3. Careful history to identify any irritants/exposures causing non-infectious cervicitis.
4. If relapse and/or reinfection with a specific STD has been excluded, BV not present, and sex partners have been evaluated and treated, and no other cause found for cervicitis, management options for persistent cervicitis are undefined. Consider a trial of antibiotic therapy for gonorrhea and chlamydia (if not previously used) with follow-up at one week to determine if resolved.
5. Women with persistent symptoms that are clearly attributable to cervicitis, consider gynecologic referral.

Epididymitis

Epididymitis is one of many diagnoses to consider when a male presents with unilateral scrotal pain and swelling. In about 10% of cases, trauma is the cause and, as an etiology, can be eliminated by history. In patients without history of scrotal trauma, differential diagnoses include: epididymitis, testicular torsion, tumor, and tuberculosis (the latter two diagnoses being less common and having typically having more indolent presentations).

Epididymitis can be divided into a sexually transmitted form frequently associated with urethritis and commonly caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae* (usually occurring in men less than 35 years of age), and a non-sexually transmitted form associated with Gram-negative bacillil such as *E. coli* or pseudomonas (usually occurring in men over 35 years of age). Of the STD-related cases, 65% to 75% are due to *C. trachomatis* (CT) and the remainder to *N. gonorrhoeae* (GC). Both of these organisms may be present in some patients, and enteric pathogens such as *E. coli* may be sexually transmitted in men who practice insertive anal intercourse.

Symptoms and signs include unilateral pain in the scrotum, tenderness, and swelling of the scrotal contents with or without urethral discharge. Epididymitis must be distinguished from testicular torsion.

Torsion generally will occur in younger men (age under 20), have a sudden onset, and present with the involved testicle lying higher in the scrotum than the uninvolved one and with the epididymis anterior instead of in its normal posterior position. Torsion is a surgical emergency so a prompt diagnosis is imperative in any man with scrotal pain and swelling.

A. Diagnosis

1. History and examination:

The approach to the diagnosis of epididymitis in patients with unilateral scrotal pain and swelling starts with ruling out trauma by history and examination.

a. Torsion should be suspected if:

- Age < 20,
- Sudden onset,
- Excruciating pain,
- Testicular elevation,

If torsion is suspected immediately refer to the emergency department for urologic consultation and radiologic studies to determine whether surgery is necessary.

b. If torsion not strongly suspected, STD-associated epididymitis becomes the most likely based on:

- Age < 35
- History of recent urethritis or dysuria,
- Gradual to sudden onset,
- Demonstrable urethritis upon examination;
- No history of underlying genitourinary pathology of any sort (prostatitis, recent catheterization, or other urologic procedure),
- And signs of epididymal or testicular inflammation (tenderness, swelling or increased warmth).

c. Men who have epididymitis related to E. coli or pseudomonas infection usually are:

- Age > 35,
- Have some form of underlying genitourinary pathology,
- Have a history of recent urological instrumentation,
- Do not have a history of antecedent urethritis, or
- Are men who practice insertive anal intercourse.

2. Laboratory:

a. If no urethral discharge is present on examination, perform a multi-stix urinalysis (urine chemstrip dipstick) for the presence of leukocyte esterase on first-void urine and/or a microscopic examination of sediment of first 10-15ml of urine for the presence of $\geq$ 10 WBC per high power field.
b. Urine-based GC/CT NAAT tests as well as all other appropriate STD screening must be done on all patients with epididymitis.
c. A midstream urine specimen should be collected and sent for culture and sensitivity to rule out infection with enteric pathogens if suspected.

B. Treatment

1. Empiric treatment in the clinic is indicated in afebrile patients with mild to moderate epididymitis before laboratory test results are available. For patients who are febrile and toxic-appearing with severe epididymitis, refer to the emergency department.

2. For cases suspected to be caused by GC and CT, the following treatment is recommended:

Ceftriaxone 250 mg intramuscularly once **and**

Doxycycline 100 mg orally twice daily for 10 days

3. For men at risk for both sexually transmitted and enteric organisms (e.g. MSM practicing insertive anal intercourse), the following treatment is recommended:

Ceftriaxone 250 mg intramuscularly once **and**

Levofloxacin 500 mg orally once daily for 10 days

4. For patients in whom only an enteric organism is suspected or who have an allergy to cephalosporins and/or tetracycline treatment with the following is recommended:

Levofloxacin 500 mg orally once daily for 10 days

5. Supportive treatment including analgesics, antipyretics, bed rest, sitz baths, and scrotal elevation should be instituted until tenderness has resolved.

C. Follow-up

Patients should return for repeat evaluation in two to three days and demonstrate symptomatic improvement. Failure to improve within three days requires re-evaluation of the diagnosis or the therapy and consideration of urologic consultation.

Patients should be followed up again after the completion of antimicrobial therapy. If swelling persists after completion of antimicrobial therapy, then referral for urological evaluation may be necessary. The differential diagnosis includes tumor, abscess, infarction, testicular cancer, tuberculous epididymitis and fungal epididymitis.

D. Counseling/Education

Patients with sexually transmitted acute epididymitis should:

1. Be counseled about epididymitis and its relationship to STDs.
2. Understand how to take prescribed oral medications.
3. Return for scheduled follow-up appointments.
4. Refer sex partner(s) in past 60 days for examination and treatment.
5. Avoid sex for > 14 days and until partner(s) are treated, and
6. Use condoms to prevent future infections.

E. Evaluation of Sex Partners

Sex partners of patients in past 60 days with sexually transmitted acute epididymitis should be evaluated for STDs and be promptly treated for gonococcal and chlamydial infections. For epididymitis related non-sexually transmitted infection or enteric organisms, evaluations of sex partners are not necessary.

Genital Ulcer Disease

Genital ulcer disease (GUD) is one of the major STD syndromes. Syndromic management is often the most practical approach to patients with GUD, given the limitations of both clinical and laboratory diagnosis. The syndromic approach is particularly useful for patients at high risk for disease, who may be lost to follow-up, and in resource-poor settings. This chapter outlines the approach to a patient in Los Angeles with a genital ulcer. Separate chapters in the STD Manual contain more detailed information on specific STD etiologies.

It has been well demonstrated that the presence of GUD increases the risk of HIV infectiousness and susceptibility, resulting in an estimated 2-5-fold increase in HIV transmission rate. It is critically important that GUD patients receive a thorough work-up and prompt treatment.

Differential Diagnosis
The most common STD etiologies of GUD are genital herpes (HSV-1 and HSV-2) and syphilis. Lymphogranuloma venereum (LGV), chancroid, and granuloma inguinale are less common.

Non-STD infectious causes of GUD include candidiasis/balanitis, scabies, and common skin infections (e.g. Staph).

Non-infectious causes of GUD include trauma/abrasions, aphthous ulcers (apthosis major), fixed drug eruptions, and Reiter's syndrome. Less common non-infectious causes are Behcet's syndrome, squamous cell carcinoma (SCC) in situ, invasive squamous cell carcinoma, and Erythema multiforme (EM)/Steven's Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN).

No etiology is found in 20% to 50% of GUD cases, most likely related to the sensitivity of the laboratory tests (affected by self-medication, duration of lesion, technology of the test).

A. Epidemiology:

In the U.S., herpes is the most common cause of STD-related genital ulcers followed by syphilis. While LGV has recently emerged (or been increasingly recognized) in the .S., the presentation encountered most frequently in recent years has been the presentation of proctitis, rather than GUD. Therefore, it is not clear that GUD (or the classic inguinal/genital presentation) due to LGV has increased. Chancroid is rare and granuloma inguinale is almost never encountered in the US: when found, both are associated with travel outside the US. Because men who have sex with men (MSM) have the highest rates of primary syphilis in Los Angeles County, GUD caused by syphilis should be the presumptive diagnosis in MSM unless another obvious etiology.

As Granuloma inguinale (GI or Donovanosis) is not covered elsewhere in the STD Manual, a brief background epidemiology is as follows: GI is caused by *Klebsiella granulomatis*, *(formerly Calymmatobacterium granulomatis).* Though almost never encountered in the U.S., GI has been found in diverse areas of the developing world, including the Caribbean. Recent outbreaks have been reported in Durban, South Africa and among the Aboriginal community in Australia. It is endemic in Papua New Guinea, parts of South Africa, India, and Brazil. Though generally sexually transmitted, transmission by fecal contamination of abraded skin and autoinoculation had been suggested.

B. Diagnosis:

1. General Considerations:

The clinical manifestations of STD-related GUD depend on the etiologic agent involved. See Table 1 on the following page.

None of these clinical signs are pathognomonic (absolutely distinctive) due to overlap and atypical presentations, except perhaps for the presence of multiple vesicles which are generally present only with HSV infection. Relying solely on clinical manifestations to determine the etiology of GUD is neither sensitive nor specific, which is why laboratory confirmation is important. Co-infections can be present in up to 10% of cases of GUD. HIV co-infected patients may have more variable signs and symptoms.

Lesions may occur anywhere in the ano-genital area, including the cervix, the vagina, the penis, around the anus and inside the rectum.

Table 1: Clinical Features of Genital Ulcers Most Commonly Seen in U.S.

	Genital Herpes	Primary Syphilis	Chancroid	LGV
Etiologic agent	HSV-1 & HSV-2	*T. pallidum*	*H. ducreyi*	*C. trachomatis* L1, L2, L3
Incubation period	2-7 days	10-90 days (avg. 21 days)	3-10 days (avg. 4-7 days)	3 days-6 weeks
Initial lesions	Papule →vesicle*	Papule	Papule or pustule	Papule, pustule, or vesicle
Presenting lesion	Vesicles	Chancre	Ulcer/bubo	Ulcer/bubo
Number and distribution of lesions	Multiple*, may coalesce. Bilateral in primary; unilateral in recurrent.	Usually one	Single or multiple	Usually one
Diameter	1-2 mm	5-15 mm	Variable	2-10 mm
Edges	Erythematous	Sharply demarcated, elevated, round, or oval	Undermined, ragged, irregular	Elevated, irregular
Depth	Superficial	Superficial or deep	Excavated, deep	Superficial or deep
Base	Serous, erythematous, nonvascular	Smooth, non-purulent, relatively nonvascular	Necrotic, generally purulent, bleeds easily	Variable, nonvascular
Induration	None	Usually present	None	Occasionally present
Pain	Common, often with prodrome of tingling*	Uncommon*	Common, severe	Variable
Lymphadenopathy	Usually present in primary infection, and absent in recurrences	Firm, non-tender, bilateral	Tender, may suppurate, usually unilateral	Tender, may suppurate, usually unilateral

*Helpful for differential diagnosis Adapted from Ballard (in K Holmes)

2. History: Historical information may assist in the determination of genital ulcer etiology. When interviewing the patient the following should be assessed:

a. Lesion history: prodrome, initial presentation (especially presence of vesicles), duration of lesion, pain, other systemic symptoms, use of systemic or topical remedies, any history of similar symptoms in the past or partners with symptoms.

b. Sexual history: gender of sex partners, number of partners (new, anonymous), venue for meeting partners/commercial sex exposure, sex for drugs or money, partners with symptoms or signs, partners with known HSV or recent syphilis diagnosis, HIV status of partners. Last sexual contact (may help to identify etiologic agent by an obvious incubation period).

c. Medical history: HIV status, skin conditions, drug allergies, medications.

d. Sexual contact outside Los Angeles County, including recent travel.

e. As always, review the patient's history of previous STDs. If patient has a history of syphilis, note the date and titer of the last RPR. If the patient was treated for syphilis elsewhere, ask the patient if s/he knows the date of the last RPR and if it was reactive. Always attempt to obtain an accurate treatment history.

3. Examination:

a. Lesion: examine for appearance, distribution, number, size, induration, depth, and tenderness.

b. Genital exam: examine genital and perianal area for other lesions. Anoscopy is appropriate in patients with rectal exposure.

c. Lymph node(s): note number and location of enlarged nodes, size, tenderness, presence of bubo.

d. General exam: thorough examination of oral cavity and skin of torso, palms and soles, and neurologic exam, including cranial nerves.

4. Laboratory: After a thorough sexual history and physical exam of the patient presenting with GUD, consider the complete differential diagnosis and conduct laboratory testing based on the probability of disease.

a. ALL patients with GUD should receive an RPR test. Consider concomitant TPPA testing if a high probability of primary syphilis and no prior history of syphilis.

b. If HSV is suspected, collect specimen from freshest lesion for HSV PCR testing.

c. If bubo present, test for LGV by sending CT culture of ulcer or bubo as well as rectal swab and urine for CT NAAT.

d. In the U.S. routine testing of patients with GUD for chancroid is not indicated. Consider if the patient gives a history of travel to an area where chancroid is prevalent. See Chancroid module for more detailed information on diagnostics.

e. Granuloma inguinale (Donovanosis or GI): The diagnosis is made by the identification of intracellular "Donovan bodies" on a biopsy or smear of lesion exudate using a Wright's stain. Lesions are slowly destructive and granulomatous. Because Wright's stain is a specialty test, providers must call STD Program and Public Health Laboratory for consultation regarding suspected GI cases.

C. Treatment of GUD

1. General approach: A diagnosis based only on medical history and physical exam is often inaccurate in diagnosing GUD. Providers, however, often need to treat before lab results are available. A decision regarding presumptive treatment depends on the probability of disease and potential loss to follow-up.

2. Primary syphilis:

Recommended:

- **Benzathine Penicillin G** 2.4 million units intramuscularly (administered as 1.2 million units in each buttock intramuscularly) once

OR

- **Alternate regimen** (See Syphilis section of the STD Manual for more detailed discussion of treatment)

Presumptive treatment is recommended if high clinical suspicion, high risk for syphilis (MSM, history of multiple partners, drug use, etc.) or risk of loss to follow-up.

3. Genital herpes: Several anti-herpetic medications are available which are equivalent in efficacy but different in their bioavailability. Treatment regimens differ for stage of disease and HIV infection. See HSV section of the STD Manual.

4. Chancroid:

Recommended:

- **Azithromycin** 1 g orally in a single dose OR
- **Ceftriaxone** 250 mg intramuscularly in a single dose OR
- **Ciprofloxacin** 500 mg orally twice daily for 3 days OR
- **Erythromycin** 500 mg orally three times a day for 7 days

In HIV-infected patients, healing may take longer, and longer courses of therapy may be required. Some experts recommend using the 7-day regimen of erythromycin for treatment of chancroid in HIV-infected persons. See Chancroid section of the STD Manual for more information.

5. LGV:

Recommended:

- **Doxycycline** 100 mg orally twice daily for 21 days

Alternates:

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

6. Granuloma Inguinale:

Recommended:

- **Doxycycline** 100 mg orally twice daily for at least 21 days and until all lesions have completely healed

Alternates: See CDC Treatment Guidelines

Treatment stops the progression of lesions. However, prolonged therapy is usually necessary to aid in granulation and reepithelialization of ulcers. Healing usually occurs inward from the ulcer margins.

Relapse can occur 6-18 months after apparently effective therapy.

D. Counseling/Education

1. Risk reduction counseling should be performed with all GUD patients:

   a. Assess patient's behavior-change potential and individualize the patient's prevention plan.

   b. Discuss prevention strategies. Educate that GUD can occur in both male or female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered. Correct and consistent use of latex condoms can reduce the risk of GUD and other STDs.

   c. Emphasize that GUD has increased risk of HIV acquisition and transmission.

2. Disease education:

   a. Provide disease-specific educational materials.

   b.. Herpes education: due to the chronicity of genital herpes, specific herpes counseling and education is important. Given the volume of information that needs to be imparted to the newly diagnosed herpes patient, it is generally advisable to bring the patient back at least once to ensure that all points are covered and that questions have been answered. See the Patient Counseling and Education section of the Genital Herpes Section.

E. Follow-up

1. All GUD patients should return to clinic in one week to evaluate lesion status and review test results. For information regarding clinical resolution and follow-up of herpes, syphilis,and chancroid see the treatment sections in the respective chapters. LGV and GI patients should be followed clinically until signs and symptoms have resolved.

2. Treat appropriately any initially untreated infections, if test results return positive.

3. GUD of undetermined cause:

   a. Review test results to see if any etiology can be determined. Note any symptomatic improvement on the empiric therapy provided at the initial visit. If symptoms are unchanged or worse, reevaluate clinical manifestations.

   b. If significant lymphadenopathy, consider LGV. If suppurative lymph nodes, also consider chancroid.

c. If ulcer(s) is deep, persists,or worsens despite therapy for syphilis, chancroid, and HSV, consider possibility of resistant *H. ducreyi*, malignancy, apthosis majore and, much less likely in the United States, Behcet's syndrome.

d. If lesions persist, but are superficial, consider fixed drug eruption, circinate balanitis (Reiter's syndrome), candidiasis, local trauma, or scabies.

e. If lesions recur and remain PCR negative, consider HSV type-specific serology.

f. If all tests were negative repeat RPR or VDRL.

g. Refer to infectious disease or dermatology if lesion(s) persist after evaluation and treatment for STD etiologies, and diagnosis is still uncertain.

F. Evaluation of Sex Partners

General: Partners should be assessed according to the diagnosis of the index patient and as described in each appropriate chapter of the manual. See HSV, syphilis, and chancroid and LGV sections of the STD Manual for more detailed information.

1. Primary Syphilis: GUD patients suspected of primary syphilis should be referred to PHI prior to discharge from the clinic for an interview regarding sexual partners who may need evaluation and epidemiologic treatment. All sex partners who were exposed within the 90 days to the case should be treated presumptively. Partners should be treated even if the initial RPR returns nonreactive.

2. LGV: Patients with suspected or confirmed LGV should be referred to the PHI prior to discharge from the clinic for an interview regarding sexual partners who may need evaluation and epidemiologic treatment. All sex partners who have had contact with the patient within 60 days before the onset of the patient's symptoms should be examined for symptoms and managed accordingly. Symptomatic contacts should be empirically treated (see LGV treatment above). Asymptomatic contacts should be empirically treated with a standard chlamydia regimen (azithromycin 1 gm orally once or doxycycline 100 mg orally twice daily for 7 days).

3. If GI is diagnosed, all sex partners of patient within the 60 days prior to onset of symptoms should be examined and offered therapy.

4. GUD of unknown etiology: Sex partners within the past three months (90 days) should be evaluated as may assist with diagnosis for both index and partner.

G. Reporting

Report suspected syphilis cases to STD Control within one working day. Suspected chancroid or LGV cases should be reported to STD Control within 7 calendar days.

Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) is a clinical syndrome resulting from the ascending spread of microorganisms from the vagina and the endocervix to the endometrium, the fallopian tubes or to contiguous structures. There are approximately one million cases in the US per year. PID may include endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Sexually transmitted organisms, especially *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, are implicated in most cases, but *Mycoplasma genitalium* has been increasingly recognized as a cause of PID. In addition, bacteria not usually associated with sexual transmission, such as anaerobes, Gram-negative rods and streptococci may also be etiologic agents. Many women with PID are asymptomatic or experience just mild-to-moderate lower abdominal pain and tenderness; indeed, many women with late complications of PID (e.g., infertility, ectopic pregnancy) report no known history of PID. Occasionally, acute infection can result in rupture of a tubo-ovarian abscess with extensive peritonitis and become life threatening. Other complications and medical consequences include chronic pelvic pain, pelvic adhesions requiring subsequent surgery, and psychological depression.

Acute PID is difficult to diagnose because of the wide variation in the symptoms and signs. Many women with PID have subtle or mild symptoms. Delay in diagnosis and treatment probably contributes to inflammatory sequelae in the upper reproductive tract. Diagnosis of PID is usually based on clinical findings.

A. Diagnosis

All young, sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence of salpingitis and endometritis. In addition, routine bimanual and abdominal exams should be done on all women with an STD, since some women with salpingitis or endometritis will not complain of lower abdominal pain.

PID is difficult to accurately diagnose, in part, because manifestations range from mild to quite severe. The clinical diagnosis should always be considered in women with cervical, uterine or adnexal tenderness. STD clinicians should maintain a low threshold for making the diagnosis of PID.

1. History:

   Patients may complain of focal or diffuse lower abdominal pain, fever, vaginal discharge, or pain with intercourse. Menstrual abnormalities, including intermenstrual and postcoital bleeding, are common. Nausea and vomiting may be present. Right upper quadrant pain is rare, but important to elicit. It may indicate the presence of generalized peritonitis and perihepatitis (Fitz-Hugh-Curtis syndrome).

2. Examination:

    a. Check temperature in patients suspected of having PID.

    b. Complete pelvic exam should be performed to assess for cervical, uterine or adnexal tenderness.

    c. Peritoneal signs (rebound, guarding) or right upper quadrant tenderness (possible Fitz-Hugh-Curtis syndrome) may be present.

3. Laboratory:

    a. Perform a pregnancy test in all patients with suspected PID.

    b. Perform a wet mount microscopy, pH and the whiff test on a sample of vaginal secretions (see criteria below).

    c. Test for gonorrhea and chlamydia.

    d. Test for syphilis and offer HIV test, according to STD clinic protocol.

4. Diagnostic criteria for empiric treatment:

Empiric treatment of PID should be initiated in sexually active young women and other women at risk for STDs who have pelvic or lower abdominal pain and no other cause for the illness can be identified, and they have one or more of the following minimal criteria:

- cervical motion tenderness *or*
- uterine tenderness *or*
- adenexal tenderness

5. Additional criteria useful in diagnosing PID:

    a. Oral temperature >38.3 C (101 F),

    b. Abnormal cervical or vaginal mucopurulent discharge*

    c. Presence of white blood cells (WBCs) on saline microscopy of vaginal secretions*

    d. Laboratory documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis*.

*The majority of women with PID have either mucopurulent discharge or WBC on wet mount microscopy. If these findings are absent, PID is less likely and other causes of pelvic pain should be investigated. Ectopic pregnancy should always be considered, even if WBC's are present on microscopy.

6. Other diagnostic criteria (not available at LAC DPH STD Clinics):

   a. Elevated erythrocyte sedimentation rate or C reactive protein (CRP).

   b. Histopathologic evidence on endometrial biopsy

   c. Tubo-ovarian abscess on sonography or CT scan

   d. Characteristic findings on laparoscopy

B. Treatment

1. *Outpatient treatment is an option in those patients:*

   a. With mild to moderate symptoms, able to tolerate oral medications, and

   b. Who are willing to return for frequent assessment..

All patients who begin outpatient treatment should be clinically re-evaluated within 72 hours and if not improved should start parenteral therapy on an outpatient or inpatient basis.

<u>Recommended outpatient regimen:</u>

- Ceftriaxone 250 mg IM once AND
- Doxycycline 100mg PO BID for 14 days AND
- Metronidazole 500 mg PO BID for 14 days.

Alternative outpatient regimens:

Due to quinolone resistant Neisseria gonorrhea, regimens that include a quinolone are no longer recommended for the treatment of PID. The following alternative regimen may be considered if the community prevalence and individual risk for gonorrhea are low. This regimen is not recommended in LAC STD clinics due to high risk of gonorrhea.

- Levofloxacin* 500 mg once daily for 14 days AND
- Metronidazole 500 mg PO BID for 14 days.

*This regimen is contraindicated in pregnant and nursing women.

If laboratory tests return indicating a gonorrhea infection, then parenteral cephalosporin is recommended. If this is not feasible (i.e. cephalosporin allergy) then azithromycin 2g orally as a single dose can be be added to the quinolone-based PID regimen.

**Fluoroquinolones may be used for PID in California if the risk of gonorrhea is low, a NAAT for gonorrhea is performed, and follow-up of the patient is considered likely. If gonorrhea is documented, change to a medication regiment that does not contain a fluoroquinolone, or obtain test-of-cure to ensure the patient does not have resistant gonorrhea. This regimen is not recommended in LAC STD clinics due to high risk of gonorrhea.

Information regarding other outpatient regimens is limited, see 2011 CDC guidelines for futher discussion.

2. *Inpatient Treatment or Hospitalization* is recommended in the following situations***:

   a. Surgical emergencies such as appendicitis or when ectopic pregnancy cannot be excluded.

   b. A pelvic abscess is suspected.

   c. The patient is pregnant.

   d. Patient compliance is uncertain.

   e. Severe illness e.g., Temp >38.3C, moderate or severe dehydration, vomiting, peritoneal signs present.

   f. The patient has failed to respond to outpatient therapy (defined below).

   ***If the patient is referred for evaluation to emergency room, treatment should be instituted before the patient leaves the STD Clinic.

C. Follow-up

Patients should be followed up three days after diagnosis (or within 2-4 days depending on which day of the week she was diagnosed), four to seven days after completing treatment, and four to six weeks after completing treatment.

Follow-up at three days should establish:

   a. Adherence to medications

   b. Symptomatic improvement

   c. Clinical improvement as documented by a repeat bimanual examination

   d. Review of lab results, especially if treated with alternate regimen

   e. Partner management

Patients who have not improved or are worse at the initial follow-up visit should be referred for hospitalization. Patients may need IV antibiotics or evaluation for other abdominal or pelvic conditions.

At the follow-up visit four to seven days after the completion of therapy, all symptoms and signs should be resolved, i.e. there should be substantial clinical improvement (e.g., absence of fever, resolution of direct or rebound abdominal tenderness, and resolution of uterine, adnexal, and cervical motion tenderness).

If patient was treated with the alternative fluoroquinolone regimen and has laboratory confirmed gonorrhea, then ceftriaxone 250mg IM should be administered. If patient cannot receive ceftriaxone, then azithromycin 2g orally should be provided.

If the patient was diagnosed with chlamydia or gonorrhea, she should be retested in three months following therapy. If an alternative regimen was used, she should return to the clinic for a test-of-cure in 3-4 weeks.

D. Counseling/Education

Patients should:

a. Be counseled about the risks of PID and routes of transmission.

b. Understand how to take prescribed oral medications.

c. Return three days after initiation of therapy for repeat evaluation.

d. Return for examination four to seven days after completing therapy.

e. Refer sex partner(s) for examination and treatment.

f. Avoid sex until patient and partner(s) have completed treatment (at least 14 days).

g. Use condoms to prevent future infections.

h. Understand the health risks of current and future episodes of PID.

i. Be advised to seek care at a hospital emergency room if there is sudden worsening of symptoms or the STD Clinic is not open.

E. Evaluation of Sex Partners

All male partners of women with PID in the last 60 days (or the last sex partner) should be examined and treated empirically for *C. trachomatis* and *N. gonorrhoeae* . PDPT should be offered to any partners unable or unlikely to present for evaluation and treatment within the week.

Proctitis

Sexually transmitted gastrointestinal syndromes can present as proctitis, proctocolitis, and enteritis. STD-related proctitis is predominantly acquired through receptive anal intercourse, and symptoms are usually present for less than two weeks. Proctocolitis and enteritis are primarily due to fecal-oral transmission during sexual practices such as anilingus. Epidemiologically, men who have sex with men represent the majority of patients presenting with these syndromes.

This section of the manual will only address the diagnosis of and treatments for proctitis. All patients who present to the STD clinic with enteric symptoms (diarrhea, abdominal cramps, etc.) should be referred to a County hospital, a comprehensive health center, or their private provider, depending on the severity of symptoms.

Proctitis is inflammation of the rectum and is associated with anorectal pain, tenesmus, and/or discharge. *Neisseria gonorrhoeae*, *Chlamydia trachomatis* (including LGV serovars), Herpes Simplex Virus types I and II and *Treponema pallidum* are the most common sexually transmitted pathogens involved.

Inflammatory STDs such as chlamydia (CT) or gonorrhea (GC) and ulcerative STDs such as herpes (HSV) and syphilis greatly increase the risk of HIV transmission. If infectious proctitis is diagnosed in an HIV-negative patient, they should be counseled about this increased risk.

A. Diagnosis

1. **History:**

    a. Patients present with rectal symptoms which include: rectal pain, tenesmus, and/or rectal discharge.

    b. Patients usually have a past or recent history of receptive anal intercourse.

2. **Examination:** Exam should include inspection of the anus and anoscopy to identify general mucosal abnormalities. Look for friability and exudate, ulcerations or fissures, as well as discrete polyps.

3. **Laboratory:** The following labs should be obtained:

    a. Rectal gonococcal NAAT*

    b. Rectal chlamydia NAAT*

    c. Rectal HSV PCR even if no obvious lesions are present.

d. Serum RPR

e. HIV test

Cultures should also be performed if they are required for medicolegal purposes.

4. **Diagnostic criteria:** Patients with a history of receptive rectal sex and signs and symptoms of acute proctitis should be presumptively diagnosed with sexually transmitted proctitis. Positive laboratory tests will confirm the diagnosis.

B. Treatment:

1. If anorectal exudate is detected on examination, patients should be presumptively treated for CT/GC proctitis. The following therapy should be prescribed pending laboratory test results:

   - Ceftriaxone 250 mg IM

     AND

   - Doxycycline 100 mg orally BID for seven days

2. Presumptive treatment for herpes and LGV should be considered if painful perianal ulcers are present or mucosal ulcers are present on anoscopy. For herpes and LGV treatment information, refer to the section of the manual for genital herpes and LGV.

3. Because there are no diagnostic tests available for LGV, patients with positive rectal CT NAAT results should receive a full 21 days of doxycycline 100mg orally BID.

4. Presumptive treatment for syphilis should be considered in patients who are contacts to syphilis and in those with the following: 1) painless perianal or anal ulcers, 2) rectal mucosal patches covered by grey mucoid exudates with an erythematous border, or 3) condyloma lata in the perianal region. In those with secondary syphilis, a skin rash and/or lymphadenopathy may also be present. For treatment of syphilis, refer to those specific sections of the manual.

C. Follow-up

1. Patients diagnosed with GC or CT should return for repeat testing (by rectal NAATs) in 3 months due to high rates of re-infection. MSM with proctitis should also be re-tested for HIV and syphilis in 3 months due to high risk for infection.
2. If the patient's symptoms of proctitis do not improve or if a non-STD cause for the rectal symptoms is suspected, the patient should be referred to gastroenterology or colorectal surgery for evaluation.

D. Counseling/Education

1. Patients should:
    a. Understand how to take prescribed medication.
    b. Refer their sex partners for evaluation.
2. Those with CT and GC proctitis should:
    a. Avoid rectal intercourse until the completion of a full course of antibiotics, and then only with condoms.
    b. Avoid receptive anilingus until the completion of a full course of antibiotics, and then use latex barriers.
    c. HIV-negative patients with rectal GC and other forms of proctitis should be counseled about their HIV risk acquisition and tested for HIV. HIV-positive clients with proctitis should be counseled about their risk of transmitting HIV during anal intercourse to their HIV negative partners.
3. HIV-negative patients should repeat HIV testing at 3 months.

E. Evaluation of Sex Partners See the sections on GC, CT, syphilis, LGV and/or HIV for information regarding the evaluation of sex partners.

F. Reporting Patients with GC, CT, syphilis and LGV should be reported using an STD CMR (see disease sections for specific instruction). HIV cases should be reported to the HIV Epidemiology Program on form DPH 8641.

Urethritis

Urethritis is characterized by a urethral discharge often accompanied by discomfort or burning with urination or urethral itching. Discharge due to gonorrhea is more likely to be purulent whereas discharge due to other causes may be mucoid or mildly purulent. It may be so scant that is only present in the mornings. However, it is not possible to differentiate gonorrhea from nongonococcal urethritis (NGU) based on clinical presentation alone.

Urethritis is commonly due to the STDs gonorrhea and chlamydia, although STD etiologies are less common among older men. *Mycoplasma genitalium* is another cause of urethritis and while FDA approved diagnostic tests for *M. genitalium* are not yet available, current standard treatments for chlamydia are also effective against *Mycoplasma*. *Trichomonas vaginalis* and HSV cause urethritis less commonly.

In addition, there is increasing evidence that oral sex can be associated with urethritis, and that Herpes Simplex Virus (HSV), adenovirus and normal oral flora may also be causative organisms. Therefore, it is possible that a patient in a monogamous relationship may develop urethritis due to receiving oral sex from his partner.

The incubation period of gonorrhea is 1-10 days (average incubation period = 2-5 days). The incubation period for other causes of urethritis may be one to five weeks, considerably longer than for gonorrheal urethritis. *Chlamydia trachomatis* has a variable incubation period of approximately 7-21 days, but may be up to several months.

A. Diagnosis

1. History:
    a. Pain or burning with urination.
    b. Purulent, mucoid, or mucopurulent urethral discharge.
    c. Patients may also present with minimal symptoms of itching/irritation at the urethral meatus.

2. Examination:
    a. Examine the urethra for discharge.
    b. If discharge is not present, have the patient strip or milk the penis to see if an exudate can be expressed.

3. Laboratory:

a. If no discharge is seen, perform a multi-stix urinalysis (urine chemstrip dipstick) for the presence of leukocyte esterase on first-void urine and/or a microscopic examination of sediment of first 10-15ml of urine.
b. Test urine and/or urethral exudate for gonorrhea and chlamydia.
c. Routine tests for HSV, or other bacterial etiologies are not recommended in the initial evaluation of urethritis but may be useful in the evaluation of patients with recurrent and persistent urethritis.

4. Diagnostic criteria: Clinicians should document that urethritis is present. Urethritis can be documented by the presence of any of the following signs:

- Mucopurulent or purulent discharge;
- Positive leukocyte esterase test on first-void urine or;
- Microscopic examination of first-void urine sediment demonstrating ≥10 WBC per high power field.

B. Treatment

1. If the patient has documented urethritis, treat the patient for chlamydia and gonorrhea (see Chlamydia and Gonorrhea sections of the manual).

2. If the diagnosis is equivocal (patient has symptoms but no signs), the decision to treat empirically vs. treat based on test results is made on a case by case basis. If follow-up is unlikely, the patient should be treated empirically for chlamydia and gonorrhea.

C. Counseling/Education

Patients treated for urethritis should:

1. Understand why they are being treated, including possible sequelae to self and partner(s) (e.g., increased HIV transmission or acquisition, PID/infertility/ectopic pregnancy in female partners).

2. Understand how to take any prescribed oral medications.

3. Return for evaluation if symptoms persist or recur after treatment.

4. Refer sex partner(s) for examination.

5. Be advised to use condoms to prevent future infections.

6. Avoid sex for at least 7 days and until partner(s) are treated (including the period when both partners are taking medication).

Patients without documented urethritis should:
1. Understand that treatment will be based on the results of laboratory tests.

2. Be told that oral sex can cause urethritis due to bacteria or viruses in the mouth of their partners, which may not be typical sexually transmitted organisms. There are no commercially available tests for most of these organisms, and no specific treatment, but symptoms are usually self-limited. Condoms should be used to decrease transmission.

D. Follow-Up for Patients Who Have Urethritis
All patients who are diagnosed with gonorrhea or chlamydia urethritis should return in 3 months for repeat testing for these organisms.

E. Partner Referral
Patients with urethritis should be encouraged to refer sex partner(s) in the past 60 days for evaluation, and testing. Because a substantial proportion of female partners of males with nonchlamydial nongonococcal urethritis are infected with chlamydia, empiric chlamydia treatment of female partners is recommended irregardless of a specific etiology in the index case. Empiric treatment of male sex partners should be based on specific etiology in the index case and/or findings on partner exam.

F. Recurrent and Persistent Urethritis
Recurrent or persistent symptoms within six weeks after treatment affect up to 20% of men with chlamydial urethritis and up to 50% of men with non-chlamydial urethritis.

Possible causes of persistent urethritis include:

- Re-infection: sex with an untreated partner or new partner or sex within 7 days of starting treatment
- Non-compliance with medications
- Persistent infection due to:
    - Inadequate drug tissue levels (e.g., prostatic involvement)
    - Resistant pathogens
    - HSV
    - T. vaginalis
    - M. genitalium
- Chronic nonbacterial prostatitis/chronic pelvic pain syndrome. This should be considered in men without any identifiable microbial pathogens experiencing persistent pain (perineal, penile, or pelvic), discomfort, irritative voiding symptoms, pain during or after ejaculation, or new-onset premature ejaculation lasting for >3 months.
- Other non-STD causes

History:

- Ask the patient about re-exposure during or after treatment, compliance with the medication, and concurrent treatment of partner(s).

Examination and Laboratory:

- Symptoms alone without documentation of urethral inflammation are not a sufficient basis for re-treatment. Establish objective evidence of urethritis by exam, leukocyte esterase test, and/or urine sediment microscopy.
- Consider wet mount microscopy of urethral discharge or urine sediment for evaluation of trichomonas infection.
- Consider HSV PCR.

Treatment for persistent or recurrent urethritis:

- Patients who did not adhere to the treatment regimen or were re-exposed to an untreated sex partner can be re-treated with the initial regimen.

  Note: If doxycycline was used as the first-line regimen, then azithromycin would be an appropriate treatment for recurrent urethritis for improved *M. genitalium* coverage.

- If the patient has persistent urethritis and has correctly completed a recommended regimen, has had his partner(s) treated appropriately, and denies re-exposure, the following regimen is recommended:

  Recommended Treatment for Recurrent/Persistent Urethritis:
  Metronidazole 2 g orally once OR Tinidazole 2g orally once
  AND
  Azithromycin 1 g orally once (if not used for initial episode).

  Notes:
  Men with a low probability of trichomonas (e.g. MSM) are unlikely to benefit from the addition of metronidazole or tinidazole.

- Moxifloxacin 400 mg orally once daily for 7 days appeared highly effective against M. Genitalium in studies involving a limited number of patients with NGU treatment failures. Moxifloxacin is very expensive and should only be used for patients with documented recurrent/persistent urethritis who have failed recommended treatment for recurrent/persistent urethritis. The use of moxifloxacin requires AMD approval.

- If suspicious of herpes urethritis, a trial of treatment for HSV can be considered, if indicated (see section on Genital Herpes for diagnosis and list of treatment regimens).

Counseling/Education

1. Explain urethritis as a syndromic disease as opposed to an infection. However, if a specific etiology is identified, discuss the routes of transmission and acquisition.
2. Explain to the patient that laboratory tests to identify all pathogens that can cause urethritis are not available.
3. Explain that oral sex can cause urethritis due to bacteria or viruses in the mouth of their partners, which may not be typical sexually transmitted organisms. There are no commercially available tests for most of these organisms, and no specific treatment, but symptoms are usually self-limited. Condoms should be used to decrease transmission.
4. Discuss the need for any female partners to be examined as pathogens may be more easily identified in the female partner (e.g. trichomonas).
5. If reinfection or non-compliance is suspected, counsel patient about the importance of abstinence, partner treatment, and completion of treatment regimen as described in the earlier section.

Partner Referral:

If men require treatment with a new antibiotic regimen for persistent urethritis and a sexually transmitted agent is the suspected cause, all partners in the past 60 days before the initial diagnosis and any interim partners should be referred for evaluation and appropriate treatment.

Medical Referral:

Referral to urology should be provided for men with pain for more than 3 months within a 6-month period for potential chronic nonbacterial prostatitis/chronic pelvic pain syndrome.

Vaginitis

Vaginitis is usually characterized by a vaginal discharge or vulvar itching and irritation; a vaginal odor may also be present. The three common diseases associated with vaginal infection include trichomonaisis, bacterial vaginosis, and vulvovaginal candidiasis or, not infrequently, a combination. Other causes of vaginal discharge or irritation include cervicitis caused by chlamydia, gonorrhea or herpes, atrophic vaginitis, allergic or irritant reactions (spermicides, deodorants, minipad adhesive), vulvar vestibulitis, lichen simplex chronicus and lichen sclerosis (especially pruritis) and foreign bodies (i.e. retained tampons).

The vagina is a dynamic ecosystem that normally contains ~10^9 bacterial colony-forming units per gram of vaginal fluid. The normal bacterial flora is dominated by lactobacilli, but a variety of other organisms, including some potential pathogens, are also present at lower levels. *Candida albicans* can also be found in normal flora as a commensal agent in 10-25% of asymptomatic women. Lactic acids and other organic acids are metabolized from glycogen by the lactobacilli, maintaining the vaginal pH between 3.8 and 4.5. The acidic environment inhibits the overgrowth of bacteria and other organisms with pathogenic potential. The normal vaginal discharge is clear to white, odorless, and of high viscosity.

History

Certain historical factors can aid in diagnosis of vaginitis.

1. Question patient about symptoms including: color and quantity of discharge, vulvar or vaginal itch, odor (particularly if fishy odor after sex), burning with urination, painful intercourse.

2. What has she done to treat the discharge and did it work?

3. Question patient regarding any history of factors adversely affecting normal vaginal flora:
    - Douching (if patient does douche, determine if she has douched within the past several hours, as this may lead to false negative findings on pH and microscopy)
    - Antibiotic or fungal therapy
    - Hormonal changes (i.e. pregnancy, menopause, oral contraceptive pills)
    - Spermicides, lubricant
    - Foreign bodies (diaphragm, IUD, tampons)
    - Menses
    - Exposure to semen (i.e. condom not used 100%).
    - Note time since last intercourse – spermicide and semen affect the pH test.

Evaluation

1. All women presenting to an STD clinic with a complaint of vaginal discharge should have a pelvic exam to evaluate the etiology of the discharge.

2. Physical exam should include a careful inspection of the external genitalia, vaginal sidewalls, and cervix, as well as of the discharge. A bimanual exam should also be performed.

    - Note character of vaginal discharge.

    - Ensure normal appearance of cervix with speculum exam to rule out cervicitis as a source of abnormal discharge.

    - Collect discharge from the lateral wall of the vagina (not from the posterior fornix, endocervix, or speculum as these can give a false pH). Determine vaginal pH with narrow-range pH paper.

    - Perform microscopic exam immediately OR emulsify specimen by immersing in test tube with 0.5 ml of sterile saline.

    - Perform amine or “whiff” test after application of 10% KOH to discharge.

    - Peform microscopic exam on two samples, one with 10% KOH and one with 0.9% normal saline.

    - Collect urine or endocervical specimen for CT/GC NAAT

    - Consider urine analysis if urinary tract infection is suspected.

    - Collect specimen for HSV PCR if HSV cervicitis is suspected or fissures/erythema seen without classic signs of candida.

Vaginitis Diagnosis

Bacterial Vaginosis is diagnosed by the presence of 3 of 4 features:

1. vaginal pH >4.5
2. thin, white/grey homogeneous discharge
3. wet mount showing >20% clue cells
4. release of a fishy odor on adding 10% KOH (the whiff test).

Vulvovaginal Candidiasis is diagnosed by the presence of budding yeast or pseudohyphae visible on KOH wet mount. Normal pH and signs of thick curdy discharge are supportive clinical signs.

Trichomonaisis is diagnosed by the presence of motile trichomonads on saline wet prep.

See individual manual sections for expanded diagnostic and treatment information.

Typical Features of Vaginitis

	Normal	BV	VVC	Trichomonaisis
Symptoms	▪ None	▪ White, thin discharge ▪ Fishy odor (particularly after sex)	▪ White thick discharge ▪ Pruritis ▪ Dysuria (external)	▪ Yellow frothy discharge ▪ Pruritis ▪ Dysuria
Findings on exam	▪ Clear to white, odorless, discharge	▪ Thin, whitish-gray homogeneous discharge	▪ Thick, curdy discharge, ▪ Vaginal erythema, ▪ Fissures	▪ Yellow frothy discharge ▪ +/- vaginal or cervical erythema
pH	≤4.5	>4.5	≤4.5	>4.5
Whiff test	Negative	Positive	Negative	Pos. or Neg.
Saline microscopy (Wet mount)	▪ PMN:EC <1 ▪ <5 wbc/hpf ▪ Rods dominate	▪ PMN: EC <1 ▪ <5 wbc/hpf ▪ Loss of rods ▪ Increased coccobacilli ▪ Clue cells (>20%)	▪ PMN:EC ratio <1 ▪ <5 wbc/hpf ▪ Rods dominate ▪ Pseudohyphae	▪ PMN:EC ratio>1 ▪ >5 wbc/hpf ▪ Mixed flora ▪ Motile trichomonads
KOH Wet mount	Negative	Negative	▪ Pseudohyphae ▪ Budding yeast	Negative

If diagnosis cannot be made after pH and microscopic evaluation consider other possible etiologies of symptoms e.g. non-infectious causes of vaginitis.

Non-Infectious Causes of Vaginitis

Irritant dermatitis/vulvitis

It is a common non-infectious cause of vulvar itching among women of all ages.
Most common irritants are: soap, bubble bath, detergents, sanitary pads, nonoxynol-9 or other spermicides, lubricants, antifungal creams, and chemically treated toilet paper.
Common allergens are benzocaine, chlorhexidine (found in KY jelly), fragrances, propylene glycol and preservatives in OTC vaginal products, latex condoms, nickel, dyes, etc.

Clinical features are indistinguishable from infectious vaginitis.

Diagnosis should be suspected in symptomatic women who do not have an otherwise apparent infectious cause.

Management:

- Identify and eliminate offending agent.
- Sodium bicarbonate sitz baths
- Corticosteroids are not recommended as they may cause local burning.

Desquamative Inflammatory Vaginitis

It is more frequently found in perimenopausal or postpartum women.
The etiology is unclear etiology, but suspected to be bacterial.

Symptoms include:
Purulent yellow-green discharge and/or dyspareunia WITHOUT signs of PID, cervicitis, or trichomonas.

Signs include:
Vestibulitis, diffuse vaginal erythema and focal erosions.

Diagnostic features:

- Vaginal pH >4.5 (usually 6 or greater)
- Negative amine test
- Many PMNs in vaginal fluids
- Increase parabasal cells and naked nuclei
- Decreased lactobacilli with replacement by Gram positive cocci

Treatment:

2% clindamycin cream intravaginally for 14 days OR
10% hydrocortisone cream 5g x 14 days.

Atrophic Vaginitis

It is most common among post-menopausal women who are not on hormone replacement therapy. Unrecognized cause in younger women with hypoestrogenic states including women who are: breast feeding, amenorrheic athletes, have ovarian nonfunction due to chemotherapy, taking tamoxifen or some women on Depo-Provera. Reduced endogenous estrogen causes thinning of the vaginal epithelium, which also lacks glycogen; this contributes to a reduction in lactic acid production and an increase in vaginal pH.

Symptoms include:

- Vaginal dryness and soreness
- Post-coital burning
- Dyspareunia
- Vaginal pruritis

Diagnostic features:

- Vagina appears pale, thin and smooth with occasional petechiae or ecchymoses. Few or no vaginal folds.
- There may be a serosanguinous or watery discharge
- pH 5-7
- Wet mount: increased PMNs with small, rounded parabasal epithelial cells. Few lactobacilli.

Treatment:

Topical vaginal estrogen, estradiol cream/tablets/ring. Refer to PMD for treatment.

Appendix (on STD Program intranet page)

Microscopic Examination, pH and Whiff Testing of Vaginal Secretions in STD Clinics

Resources available on STD Program Intranet Site

Resources available on the STD Program Intranet Site

STD Program

- How To Contact the STD Program
- Map and Directions to the STD Program
- STD Program Website (link)

LA County STD Clinics

- Definition of New/Return STD Patient Visit - summary sheet
- What to Expect From Your Visit Leaflet (English) (Spanish)
- Staff & Managers by STD Clinic
- Clinic Schedule
- Clinic Reports
- SPA/STD Improvement Issues & Draft Documents

Staff Education, Trainings & Meetings

- STD Program Medical Inservice Schedule
- Workshop Schedule & Registration Form
- Inservice Map, Barlow Respiratory Hospital
- Inservice Map, Ferguson Auditorium

Core STD CME Presentations

- Congenital Syphilis, Sept. 06 Helene Calvet
- Chlamydia, Gonorrhea and Related Syndromes, Jan. 07 Sarah Guerry
- Emergency Contraception, Feb.07 Sarah Guerry
- Advances in Genital Herpes: Diagnosis, Treatment, and Prevention, Feb. 07 Sarah Guerry
- Sexual Risk Assessment and Risk Reduction Counseling, Jan. 07 Linda Creegan
- HPV, Jan. 07 Helene Calvet
- Pap Training for MDs July 09 Pomerance
- PDPT, May 07 Tracie McClain
- Syphilis, Nov. 08 Christine Wigen
- Cervicitis, May 09 Sarah Guerry
- Urethritis, May 09 Christine Wigen
- Cervical Cancer and Screening Feb. 09 Singhal

Treatment Guidelines

- CDC Treatment Guidelines 2010
- California STD Treatment Guidelines for Adults and Adolescents 2010
- California Guidelines for Chlamydia and Gonorrhea Field Delivered Therapy

STD Clinic Manual

- STD Clinic Manual – Printed Version
- STDs by Disease
- STDs by Syndrome

STD Clinic Resources

- Anal Intercourse Study
- Ceftriaxone and Lidocaine Intramuscular Injection Protocol
- Emergency Contraception (EC) & Birth Control
- Forms / Labels
- Health Education Materials
- Hepatitis Vaccine Information
- HIV PreExposure Prophlaxis (PrEP)
- Laboratory
- Nurse Directed Clinic Pilot Project at Hollywood Wilshire STD Clinic
- Nurse STD Screening Clinic (NSC) Antelope Valley
- Paps
- Patient Delivered Partner Therapy (PDPT)
- Pharmacy
- Referrals
- Safety of Common STD Medications in STD Pregnancy
- STD Reporting
- Telephone Results
- Voicemail Script for STD Clinics

Folders in STD Clinic Resources

Anal Intercourse Study

- Recruitment Script
- Palm Card
- Locator Form

Emergency Contraception (EC) & Birth Control

- Birth Control Methods Leaflet B515 (English)
- Birth Control Methods Leaflet B515S (Spanish)
- EC in STD Clinics Policy 317
- EC Protocol
- EC Provider Information Sheet
- EC Patient Information Leaflet (English)
- EC Patient Information Leaflet (Spanish)
- EC Patient Education Order Form
- Family Planning Services, listed by STD Clinic Area (English)
- Family Planning Services, listed by STD Clinic Area (Spanish)

Forms / Labels

- Prepack Meds. Order Form
- Syphilis Record Card (H-3037) FAQs and Examples
- Gonorrhea Partner Cards
- Instructions for Completing H2541
- STD Clinic Intake Form H-2541
- Mailing label Template for copy of H2541 (Avery 5160)
- STD Clinic Return Clinic Visit / Phone Result Appointment Form H2542
- CMR Form for STDs
- CMR form and reporting instructions for other communicable diseases ACD
- CMR form and reporting instructions for HIV
- STD Clinic Pharmacy Px Order Form
- Hepatitis Vaccine Referral Form
- PDPT Medication Labels - Template Avery 5160
- Health Education Materials Order Forms
- Adult Hepatitis Vaccine Order Form

Hepatitis Vaccine Information

General

- Hepatitis A & B Vaccination - guidelines and screening questions
- Guidelines for Hepatitis A, B & C Serologic Tests in CHS STD Clinics - from 3/15/08
- Hepatitis Vaccine Referral Form
- LAC/DHS Gastroenterology & Liver Referral Resources
- LAC Immunization Program Hep A Info. Sheet
- LAC Immunization Program Hep B Info. Sheet
- CMR for Reporting Acute and Chronic Hepatitis B to ACD Program
- Adult Hepatitis Vaccine Order Form

Hepatitis & Vaccine Q & A for Public & Professionals

- Hep A Vaccine & Disease Q & A
- Hep B Vaccine & Disease Q & A

Vaccine Information Statements (VIS)

- How to Obtain VIS in other languages
- VIS Hepatitis A English
- VIS Hepatitis A Spanish
- VIS Hepatitis B English
- VIS Hepatitis B Spanish

Laboratory

- Guidelines for Hepatitis A, B & C Serologic Tests in CHS STD Clinics - from 3/15/08
- PH Laboratory Departmental Phone List
- Instructions for Neisseria gonorrhoeae cultures
- STD Specimen Handling and Ordering Guide
- PHL letter - New HIV & Hepatitis Tests
- Instructions for Chancroid Culture
- Examination of Vaginal Wet Preps (Video)
- Microscopic Examination, pH and Whiff Testing of Vaginal Secretions in STD Clinics
- Chlamydia and Gonorrhea Testing using Self Collected Vaginal Swabs: STDP Recommendations
- Instructions for self-collected vaginal swabs - English and Spanish
- New Method of Testing For Herpes Simplex Virus (HSV)

Nurse Directed Clinic Pilot Project at Hollywood Wilshire STD Clinic

- Nurse Directed Clinic Protocol
- Patient Flow Diagram
- Chart Intake Form
- Clinic Flow Survey form
- Flow Analysis Checklist
- Patient Information Leaflet (HW ND version)
- Patient Satisfaction Survey Form (English)
- Patient Satisfaction Survey Form (Spanish)
- Protocol for Specimen Collection for Routine Testing in STD Clinic
- Self Administered Questionnaire - Patient copy English
- Self Administered Questionnaire - Clerks copy English
- Self Administered Questionnaire - Patient copy Spanish
- Timeline
- Training Presentation

Nurse STD Screening Clinic (NSC) Antelope Valley

- CT/GC testing/screening guidelines
- Hepatitis testing/screening guidelines
- Instructions for taking a rectal swab - English and Spanish in a single document
- NSC New Patient Clinic Flow Chart
- NSC Poster - English
- NSC Screening Clinic Protocol
- NSC Self-administered questionnaire - English Spanish
- NSC Signed protocols
- NSC Testing Protocol
- NSC Treatment Protocol
- Throat swab training powerpoint

Paps

- Pap Protocol
- STD Clinic Pap Data 2010
- Pap Tracking Log BLANK
- Pap Tracking Log SAMPLE Appx B
- Colposcopy Referral Table Appx F
- Pap Processing - Quick Reference Guide
- Actinomycosis-like organisms on Pap Tests
- Foundation Laboratory Pap Request Form SAMPLE

Pap Result Letters

- Pap Result Letters
- Pap Result Letter SAMPLE Appx C

Pap Patient Information Materials

- Pap Test Patient Handout (English) (Spanish) Appx A
- HPV Basics Brochure B-521 (English) (Spanish) Appx D
- Colposcopy Information Sheet (English) (Spanish)
- DHS Clinic and Hospital No-Cost and Low-Cost Information and Forms

Pap Training

- Pap Training for Clinic Nurses, PHNs and PHIs July 09 (Slides) (Handouts)
- Pap Training for MDs July 09 Pomerance (Slides) (Handouts)
- Cervical Cancer and Screening Feb. 09 Singhal (Slides) (Handouts)

National Pap Guidelines

- ACOG Cervical Cytology Screening Bulletin 2009
- 2006 Consensus guidelines for the management of women with abnormal cervical cancer screening tests
- ACS Cervical screening guidelines
- ASCCP Cervical cytology algorithms

Patient Delivered Partner Therapy (PDPT)

- Prepack Meds. Order Form
- PDPT Policy: 314 - Patient Delivered Partner Therapy for Chlamydia and Gonorrhea
- PDPT Protocol
- PDPT Medication Label Template
- CDC letter on Expedited Partner Therapy 05/11/05

Brochures & Leaflets

- Gonorrhea/chlamydia PDPT information brochure (English B516) (Spanish B516S)
- Chlamydia only PDPT information brochure (English B517) (Spanish B517S)

Pharmacy

- Treatment leaflets for clinics with PILS
- Treatment leaflets for clinics without PILS
- STD Clinic Pharmacy Px Order Form
- PDPT Prepack Meds. Order Form
- PDPT Medication Label Template
- Safety of Common STD Medications in STD Pregnancy
- Memo - metronidazole tablet shortage 02/16/11

Referrals

- Family Planning Services, listed by STD Clinic Area (English) (Spanish)
- Court Ordered HIV Testing & Counseling Sites
- LAC/DHS Gastroenterology & Liver Referral Resources
- Lumbar Puncture Referral Resource
- Addiction CME handout
- Self-help Group Information

STD Reporting

- CMR Form for STDs
- STD Reporting Instructions

Telephone Results

- CHS Policy 318 - Provision of STD Laboratory Results by Telephone
- Protocol - Provision of STD Laboratory Results by Telephone
- Telephone Result Appointment Card Template