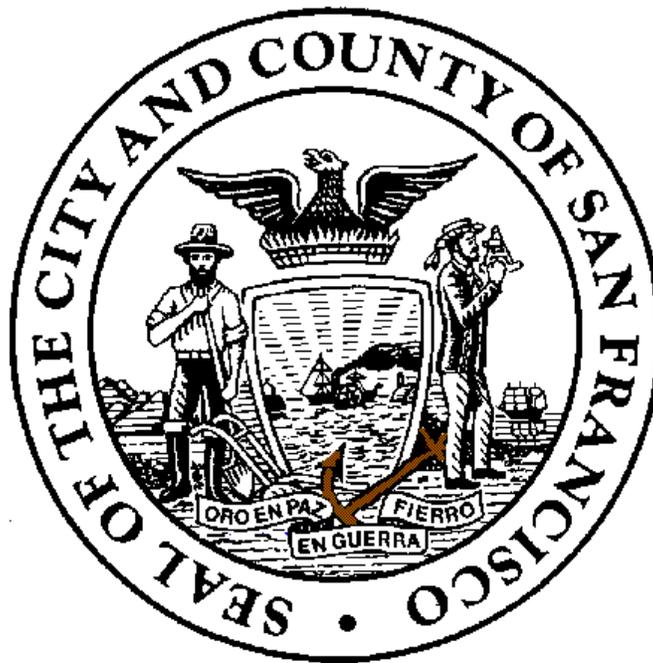


SAN FRANCISCO CITY CLINIC

CLINICAL PROTOCOLS

SEXUALLY TRANSMITTED DISEASES



Sexually Transmitted Diseases Prevention and Control Services

San Francisco Department of Public Health

San Francisco, California USA

May 2017

**SAN FRANCISCO CITY CLINIC
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Actinomycosis in Women with IUD

Actinomyces israelii is a fastidious, anaerobic Gram-positive bacterium that can colonize the female genital tract and may be detected on a Pap smear. While usually harmless, *Actinomyces* can cause a rare but serious form of PID in IUD users. This condition, called “pelvic actinomycosis,” is typically indolent and characterized by fever, abdominal pain, weight loss, and abnormal vaginal bleeding or discharge.

While pelvic actinomycosis is rare, detection of *Actinomyces* on Pap smear in IUD users is not. There is no clear-cut standard of care in asymptomatic women, but evidence suggests that neither IUD removal nor antibiotic therapy is needed. If a patient’s Pap smear shows actinomyces, she should be informed and examined. Symptomatic cases should be evaluated individually and may require consultation with the attending physician.

A. Diagnosis

1. History
 - a. *Actinomyces* noted on a Pap smear of IUD user.
 - b. Evaluate for signs of pelvic infection; lower abdominal tenderness, cervical motion tenderness, uterine/adnexal tenderness, fever, weight loss, abnormal vaginal bleeding or discharge (see [PID](#)).
2. Laboratory
 - a. Test for gonorrhea and chlamydia per San Francisco City Clinic guidelines.

B. Treatment

1. For an asymptomatic patient:
 - a. Removal of IUD is not necessary.
 - b. Antibiotic treatment is not necessary.
 - c. Patient should be counseled regarding signs and symptoms of pelvic actinomycosis and informed that she should be evaluated if any such symptoms develop.
2. If patient has symptoms of PID, refer to SFGH ER for further management after standard PID treatment started at San Francisco City Clinic. The treatment for actinomyces is usually IV antibiotics. The IUD will be removed following antibiotic administration and should be sent for anaerobic culture.
3. If patient has cervicitis, evaluate and manage as per [cervicitis protocol](#).

Bacterial Vaginosis

Bacterial vaginosis (BV) is a polymicrobial syndrome that results from alterations in the normal vaginal flora. In BV, anaerobic bacteria replace the normal hydrogen peroxide producing *Lactobacillus sp.* that colonize the vagina. *Gardnerella vaginalis* (a small Gram-negative pleomorphic coccobacillus), *Bacteroides sp.* (anaerobic Gram-negative bacilli), *Mobiluncus sp.* (motile, anaerobic, curved Gram-positive bacilli), and genital mycoplasmas have been implicated. Molecular investigations have also found novel bacteria that are highly specific for BV. BV is manifested by a malodorous vaginal discharge that is often most noticeable after intercourse and has been associated with subclinical endometritis and pelvic inflammatory disease. Women with BV may be at increased risk for other STDs (e.g., HIV, gonorrhea, chlamydia and HSV-2). Treatment of male sex partners has not been beneficial in preventing BV recurrence.

A. Diagnosis

1. History

- a. Patients often complain of a malodorous vaginal discharge (may have a fishy odor, usually not itchy).
- b. Patients may be asymptomatic, but have all the signs of BV on exam.
- c. Douching is associated with BV.

2. Examination

- a. Classically, BV produces a homogeneous, adherent, malodorous, white vaginal discharge.
- b. In the absence of other conditions, the remainder of the exam is normal.

3. Laboratory

- a. BV can be diagnosed by clinical criteria (Amsel's) or by Gram stain (Nugent criteria).
- b. Amsel's criteria (at least 3 must be present):
 1. Homogeneous gray or white, adherent discharge on the vaginal wall.
 2. pH of vaginal secretions > 4.5.
 3. A positive whiff test: fishy, amine odor from vaginal fluid, enhanced by mixing with 10% potassium hydroxide (KOH).
 4. Presence of clue cells on a saline preparation. Clue cells are epithelial cells with a granular appearance and obscured edges caused by adherent bacteria.

- c. Nugent criteria: Standardized 0-10 point score based on Gram stain that is based on the relative concentration of lactobacilli (i.e., long Gram-positive rods), Gram-negative and Gram-variable rods and cocci (i.e., *G. vaginalis*, prevotella, porphyromonis, and peptostreptococci) and curved Gram-negative rods (i.e., mobiluncus).
- d. Vaginal swab for trichomoniasis nucleic acid amplification test (NAAT) (if available).

B. Treatment

a. Non-pregnant Women

The goal of treatment is to relieve signs and symptoms. At this time, evidence does not support treating asymptomatic women.

Recommended regimens:

1. **Metronidazole** 500 mg orally twice daily for 7 days *OR*
2. **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally daily for 5 days *OR*
3. **Clindamycin** cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days (patients should be told this is an oil-based cream, and can weaken latex condoms and diaphragms for 5 days after use)

Alternative regimens:

1. **Clindamycin** 300 mg orally twice daily for 7 days (note: keep in mind small risk of antibiotic-associated colitis) *OR*
2. **Clindamycin Ovules** 100 g intravaginally once at bedtime for 3 days (patients should be told that ovules are oil-based, and can weaken latex condoms and diaphragms for 5 days after use), *OR*
3. **Tinidazole** 2 g orally once daily for 2 days *OR*
4. **Tinadazole** 1 g orally once daily for 5 days

b. Pregnant Women

Although BV has been associated with preterm labor and other adverse pregnancy outcomes, the mechanism remains poorly understood, and treating asymptomatic BV diagnosed during pregnancy has not been shown to decrease the risk for these events. Therefore treatment of asymptomatic BV during pregnancy is not recommended. Treatment of symptomatic BV during pregnancy is indicated to reduce the signs and symptoms of vaginal infection.

Multiple studies have failed to demonstrate an association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns. Oral therapy has not been shown to be superior to topical therapy for treating BV during pregnancy. Pregnant women can therefore be treated with either of the oral or vaginal regimens recommended for non-pregnant women.

C. Follow-up

Routine follow-up is not recommended for non-pregnant women. Recurrence is common (up to 30% of women will have a recurrence within 3 months), and women should be advised to return for re-evaluation if symptoms recur. Alternative treatment regimens may be used to treat recurrent disease (see below).

D. Counseling/Education

Patients should:

1. Understand how to take prescribed medications and be instructed to avoid alcohol 24 hours before and after metronidazole administration.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refrain from douching.
4. Be offered condoms and advised that condoms may be helpful to reduce the frequency of recurrence.
5. Be screened for HIV and other STDs according to current clinic guidelines.

E. Evaluation and Treatment of Sex Partners

No clinical counterpart of BV is recognized in the male and treatment of sex partners does not affect likelihood of relapse or recurrence. The male partner can be offered a STD exam and appropriate screening tests and be given relevant information on BV. Female partners of females diagnosed with BV have shown high rates of BV in several studies and should be offered an evaluation and STD testing as indicated by screening guidelines.

F. Special Considerations

Recurrent BV

Recurrent BV is common. For women with recurrent BV a longer course of therapy (10-14 days) may be helpful.

With multiple recurrences, consider prophylactic use of either:

1. **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally at bedtime twice weekly for 4-6 months *OR*
2. **Metronidazole** 2 g orally plus **fluconazole** 150 mg orally once monthly for 6 months

Candida Balanitis

In men, the glans of the penis may become colonized with yeast. This condition (candida balanitis) typically causes pruritis and a red rash with white flat lesions on the glans, prepuce, coronal sulcus, and shaft. If inflammation continues, men may exhibit shallow ulcerations on the glans. As in women, this condition is generally not sexually transmitted, partner referral is not necessary and no data support the treatment of sex partners. After unprotected intercourse with a woman who has *Candida vaginitis*, a man may experience transient erythema, burning, and pruritis on the glans of the penis. This may occur as early as minutes after intercourse, and may be alleviated by washing. Candida balanitis is more common and more frequently symptomatic in uncircumcised men and is more common in men with diabetes mellitus.

A. Diagnosis

1. History
 - a. Rash on glans and/or prepuce.
 - b. Often pruritic.
 - c. More common in men whose partners have recurrent vaginal candidiasis
 - d. More common in men with diabetes mellitus or immunosuppression, including HIV infection.
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.
 - b. If there is any question of diagnosis, a stat RPR and VDRL (or RPR) must be done to exclude syphilis.
 - c. Consider herpes simplex virus (HSV) serology and/or HSV PCR.
4. Diagnostic Criteria
 - a. History and clinical appearance consistent with above or
 - b. A KOH preparation from a skin scraping which reveals budding yeast and/or pseudohyphae.

B. Treatment

Any of the following topical OTC antifungal preparations are effective:

1. **Clotrimazole** 1% cream twice daily x 7-14 days
2. **Miconazole** 2% cream twice daily x 7-14 days
3. **Tolnaftate** (tinactin) 1% cream twice daily x 7-14 days

All are available without prescription. Creams should be applied in a thin layer twice a day until balanitis has resolved. Most cases should resolve within one to two weeks. Therapy may require up to a month in some cases. The area under the prepuce should be kept clean and dry.

Severe disease:

Fluconazole 150 mg orally once, then repeated in three days

Other oral azole agents such as ketoconazole and itraconazole have been shown to be as effective as topical agents; one advantage is ease of administration but the potential for toxicity, particularly adverse hepatic effects should be considered.

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 offered 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. A primary care provider should evaluate patients if glucosuria is present.

Candidiasis in Women

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

A. Diagnosis

1. History
 - a. Patients may complain of vaginal discharge, vaginal/vulvar itching, vaginal soreness, external dysuria or dyspareunia.
 - b. Note recent use of antibiotics, 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.
3. Laboratory
 - a. Budding yeast and/or pseudohyphae on a saline or KOH preparation.
 - b. 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 stain, potassium hydroxide wet mount preparation (10% KOH), or saline wet mount.
 - b. The pH is usually in the normal range of 4.0 to 4.5.
 - c. Mixed infection can occur so patients should also be evaluated for other causes of vaginitis.

B. Treatment

Any of the following antifungal preparations are effective:

Vaginal:

1. **Clotrimazole** 1% cream 5 g intravaginally for 7-14 days
2. **Clotrimazole** 2% cream 5 g intravaginally for 3 days

3. **Miconazole** vaginal suppositories (100-200 mg) or cream (2%, 4%) x 3-7 days
4. **Terconazole** vaginal suppositories (80 mg) or cream (0.4%, 0.8%) x 3-7 days
5. **Butoconazole** 2% cream 5 g intravaginally in a single application
6. **Tioconazole** 6.5% ointment 5 g intravaginally in a single application

Oral:

1. **Fluconazole** 150 mg orally once – do not use in pregnancy

Severe candidiasis may be treated with Fluconazole 150 mg orally repeated in three days.

Note: Single-dose therapy of vaginal creams has higher failure rates than three or seven day regimens. Clotrimazole and miconazole are available without prescriptions. Vaginal creams and suppositories are considered safe in pregnancy and during lactation.

Fluconazole (or other oral azoles) should not be used in pregnancy.

Other oral azole agents such as ketoconazole and itraconazole have been shown to be as effective as topical agents; one advantage is ease of administration but the potential for toxicity, particularly adverse hepatic effects, should be considered.

C. 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) (see [section F](#)).

D. Counseling/Education

Patients should:

1. Understand how to take or use medications.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Understand that many yeast creams are oil-based and may break down latex condoms or diaphragms.
4. Be screened for HIV and other STDs according to current clinic guidelines.

E. Evaluation and Treatment of Sex Partners

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

F. Special Considerations

Recurrent Candidiasis

Defined as four or more recurrences per year. Due to poor accuracy of self-diagnosis (confusion with other causes of vaginitis) it is recommended that recurrences be clinician-diagnosed.

First, try a longer duration of initial therapy before initiating a maintenance antifungal regimen: e.g., 7-14 days of topical therapy or fluconazole 200 mg orally every third day for a total of 3 doses (day 1, 4 and 7).

If a longer duration of therapy is unsuccessful, consider a maintenance regimen (continue for 6 months, then trial period off therapy):

Fluconazole 100-150 mg orally weekly x 6 months

(Consider giving fluconazole 150 mg q72h x 3 doses prior to starting the weekly dosing regimen)

If this is not feasible, topical treatments administered intermittently can be used as a maintenance regimen.

Fluconazole is not effective against *Candida glabrata* which has been found in some studies to be present in HIV-infected women, sex workers, and women with multiple partners. This pathogen requires longer duration of treatment (7+ days) with intravaginal antifungal creams or other oral medications. Consult with the attending physician in difficult cases, as fungal cultures may be required.

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. Chancroid does not have a vesicular stage but may present initially as a small pustule or as a raised, beefy red lesion. Unilateral or bilateral tender adenopathy occurs in approximately half the patients and an inguinal bubo (abscess) 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. Complications of chancroid include phimosis or paraphimosis and ruptured buboes, which may result in fistulae. Studies from Africa, where chancroid was once endemic, suggest that genital ulcer disease caused by *H. ducreyi* increases risk of HIV transmission. Genital ulcers caused by *H. ducreyi* are **extremely rare** in the United States (and in San Francisco).

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 vulvar or vaginal ulcer(s) or with dysuria, bleeding, or vaginal discharge. Ulcer(s) in women may be relatively painless.
- b. See [genital ulcer disease section](#) for key characteristics that should be ascertained during the history of present illness (HPI).

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, has undermined edges that can be ragged or serpiginous in appearance.
- c. Rectangular shaped ulcers are considered characteristic. The ulcers are usually sharply demarcated, but they may become confluent and quite large.
- d. They are generally not indurated, and are usually friable and deep. The base may be covered by a grey or yellow necrotic purulent exudate.
- e. Tenderness is usually, although not always, present.
- f. Painful and tender inguinal adenopathy is present in approximately 50% of patients.
- g. 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.
- h. See [genital ulcer disease section](#) for key characteristics that should be ascertained during the exam.

3. Laboratory

- a. Since ≥ 1 organism may coexist in a genital ulcer, all patients with a genital ulcer must have a darkfield examination.
- b. If the darkfield examination is negative, a stat RPR, and lab-based TPPA and VDRL (or RPR) should be obtained. In addition, a swab from the ulcer should be sent for an HSV PCR.

4. Diagnostic Criteria

- a. Definitive diagnosis requires the identification of *H. ducreyi* on special culture media. This is not widely available (and at this time is not available at City Clinic)
- b. Suspect chancroid is defined as a painful ulcer on the genitalia accompanied by enlarged and tender inguinal lymph nodes, with other causes of genital ulcer disease ruled out.
- c. *All suspected cases of chancroid should be presented to the attending physician.*

B. Treatment

Recommended regimens:

1. **Ceftriaxone** 250 mg IM once *OR*
2. **Azithromycin** 1 g orally *OR*
3. **Ciprofloxacin** 500 mg twice daily for 3 days *OR*
4. **Erythromycin** base 500 mg three times daily for 7 days

Note: Ceftriaxone and azithromycin offer the advantage of directly observed administration at the clinic. There have been no documented cases of ceftriaxone or azithromycin-resistant H. ducreyi.

Buboes should be drained to prevent rupture and subsequent fistula formation. This can be performed by the attending physician in the clinic with a 20 gauge, 1 1/2 inch needle and syringe. First, cleanse skin with povidone-iodine or chlorhexidine. To avoid creating a sinus tract, insert needle into unaffected skin adjacent to area of bubo involvement, then direct needle into bubo and aspirate contents.

C. Follow-up

Patients with presumed or confirmed chancroid should be re-examined three to seven days after beginning therapy. If treatment is successful, lesions should be less painful within three days 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. The clinical resolution of lymphadenopathy is slower than that of ulcers. A bubo may continue to enlarge even after successful therapy of the ulcer, so careful follow-up of a bubo is necessary and the attending physician should be informed of any buboes.

Patients should have a non-treponemal antibody test (VDRL or RPR) repeated one week and six weeks after therapy. HIV-testing should be encouraged in any patient with negative or unknown HIV serostatus at the time of the visit. If there is no improvement at the 1-week follow-up, the attending physician should be informed.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Avoid sex for at least 7 days and until the patient and partner(s) have completed therapy and the ulcer(s) are totally healed.
3. Be offered condoms and advised that condoms can prevent future infections.
4. Be referred to the disease control investigator (DCI) for counseling and interview.
5. Be screened for HIV and other STDs according to current clinic guidelines.
6. Be counseled about PrEP if at elevated risk for HIV-infection

E. Evaluation and Treatment of Sex Partners

Partners who had sexual contact with the patient during the 10 days preceding the patient's onset of symptoms should be empirically treated with an appropriate regimen for *H. ducreyi*.

Chlamydia Trachomatis

Chlamydial genital infection is one of the most common 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. An obligate intracellular bacterium, *Chlamydia trachomatis* (CT) can infect the urethra, cervix, rectum, and less commonly, the pharynx. Infections in both women and men commonly occur without symptoms or signs. Women may report urinary frequency and dysuria, an increase in vaginal discharge, or lower abdominal pain. Men may have symptoms that include urethral itch, dysuria, or a mucoid-to-purulent discharge. Rectal chlamydia infection is usually asymptomatic, but can be associated with symptoms of proctitis, including anorectal pain, discharge or tenesmus. Serious complications related to chlamydial infection include epididymitis in men; endometritis, salpingitis, infertility, ectopic pregnancy, chronic pelvic pain and postpartum infection in women; and conjunctivitis and pneumonia in infants. Chlamydia has a variable incubation period of approximately 7-21 days, but symptom onset may be delayed up to several months. [Lymphogranuloma venereum \(LGV\)](#), an uncommon disease caused by *C. trachomatis* serovars L1, L2 or L3, will be discussed in another 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 many men (> 50%) may be asymptomatic. Rectal chlamydial infections may be asymptomatic, or may resemble gonococcal proctitis with pain, bleeding, tenesmus or mucous discharge, particularly when caused by LGV-serovars of *Chlamydia* (see [LGV](#)).
- b. Female patients may have no symptoms. If symptomatic, women may complain of vaginal discharge, urinary frequency and dysuria, or lower abdominal pain.
- 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. Male patients with rectal chlamydia may have signs of proctitis, although the exam may be normal (see [proctitis](#) and [LGV](#)).
- c. Female patients may have mucopurulent cervical discharge, cervical erythema, edema, and friability, although the exam may be normal.

3. Laboratory

- a. A nucleic acid amplification test (NAAT) is the preferred screening test for anal or genital chlamydia infection and can be performed from urine, vaginal, urethral, cervical or rectal samples. In women, a self-collected or provider-collected vaginal swab is the specimen of choice. A urine specimen can be tested if there is a tampon in place or the patient is unwilling or unable to have a vaginal swab collected. Labs that have met CLIA requirements and validated chlamydia NAAT testing from extragenital sites can perform a chlamydia NAAT test on an oropharyngeal or rectal sample.
- b. The Centers for Disease Control (CDC) recommends annual chlamydia screening of sexually active women ≤ 25 years. Rectal screening is recommended for men who report receptive anal sex. Women who have undergone hysterectomy with complete cervical resection need not be screened. See current clinic guidelines for specific recommendations regarding indications for genital and extragenital chlamydia screening.
- c. Diagnostic testing should be performed for all individuals with syndromes potentially caused by chlamydia including urethritis, epididymitis or proctitis in men, and vaginitis, cervicitis, PID, dysuria, pyuria and intermenstrual bleeding in women.

4. Diagnostic Criteria

- a. Positive test by NAAT of urine, cervical, vaginal, rectal, pharyngeal or urethral specimens **or**
- b. A positive chlamydia culture from the cervix, vagina, rectum, pharynx or urethra.

B. Treatment

a. Uncomplicated Chlamydia Infections*

Recommended regimens:

1. **Azithromycin** 1 g orally in a single dose *OR*
2. **Doxycycline** 100 mg orally twice a day for 7 days

Alternative regimens:

1. **Erythromycin** base 500 mg orally four times a day for 7 days *OR*
2. **Erythromycin ethylsuccinate** 800 mg orally four times a day for 7 days *OR*
3. **Ofloxacin** 300 mg orally twice a day for 7 days *OR*
4. **Levofloxacin** 500 mg orally once daily for 7 days

*Note that patients with symptomatic rectal Chlamydia (e.g. rectal pain or discharge in the setting of a positive rectal CT NAAT) should be evaluated for LGV. In this scenario,

strong consideration should be given to empiric treatment for LGV with doxycycline 100 mg PO BID x 21 days. See sections on [proctitis](#) and [LGV](#).

b. Pregnant Women

Doxycycline, ofloxacin and levofloxacin are contraindicated in pregnant women. Clinical experience and preliminary data support that azithromycin is safe and effective in pregnancy. All pregnant women with Chlamydia should have a test of cure 3-4 weeks after treatment.

1. **Azithromycin** 1 g orally in a single dose

Alternative regimens for pregnant women:

1. **Amoxicillin** 500 mg orally three times a day for 7 days
2. **Erythromycin base** 500 mg orally four times a day for 7 days *OR*
3. **Erythromycin base** 250 mg orally four times a day for 14 days *OR*
4. **Erythromycin ethylsuccinate** 800 mg orally four times a day for 7 days *OR*
5. **Erythromycin ethylsuccinate** 400 mg orally four times a day for 14 days

Erythromycin (base or ethylsuccinate) may have gastrointestinal side effects that discourage patient adherence and therefore lower efficacy.

C. Follow-up

1. Note that for 3 weeks after completion of therapy, nonculture tests (e.g., NAATs) may detect biologically inactive *C. trachomatis* DNA and may yield false-positive results.
2. If a patient is being evaluated for re-infection or treatment failure and it has been less than 3 weeks since the initial treatment, testing with a nonculture method is not recommended. If there is strong suspicion of nonadherence or of re-infection, repeat empiric treatment should be given. Test-of-cure at three weeks is only indicated in pregnant women. All patients diagnosed with chlamydia should have repeat testing at 3 months to rule out re-infection. Re-infection in patients treated for chlamydia is common (10-15%).
3. There are increasing observational data suggesting that **azithromycin** may be inferior to **doxycycline** for rectal Chlamydia. For individuals with rectal Chlamydia who have a positive test 3 months after treatment with azithromycin, we recommend treating with **doxycycline** 100 mg orally twice daily x 7 days, especially if suspicion for re-infection is low.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Return for evaluation if symptoms persist or recur after treatment.

3. Be counseled to notify sex partners from the past 60 days and refer them for examination and treatment, or provide them with patient-delivered partner therapy.
4. Avoid sex for at least 7 days and until partner(s) have completed therapy.
5. Be advised to return in 3 months for repeat testing to rule out re-infection.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Understand the importance of regular screening (if the patient is a man who has sex with men (MSM) or age \leq 25 years) since chlamydia is often asymptomatic.
8. Be screened for HIV and other STDs according to current clinic guidelines.
9. Be counseled about PrEP if at elevated risk for HIV-infection (note that PrEP should be recommended to MSM, trans women and trans men who are HIV-negative and have rectal Chlamydia).

E. Evaluation and Treatment of Sex Partners

All sex partners within the prior 60 days of patients who have *C. trachomatis* infection should be examined, tested, and empirically treated with an appropriate regimen. Patient or field-delivered therapy with **azithromycin** 1 g orally once or **doxycycline** 100 mg orally twice a day for 7 days may be treatment options for partners unlikely to come in for examination.

Patients should be instructed to refrain from having sex for one week after treatment is initiated, and should not resume sexual activity with their partner until one week after the partner initiates treatment. Some patients think that it is safe to have unprotected sex if both they and their partner(s) are taking medication simultaneously. Even if a one-time dose of medication is prescribed patients should be instructed to avoid sex for 7 full days.

F. Special Considerations

Reporting

Report confirmed or suspected chlamydia cases to STD Control within 1 week.

Epididymitis

Acute 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 urinary tract infections (e.g. *E. coli*) that usually occurs in men over 35 years of age. Acute epididymitis caused by enteric organisms also occurs in men who have insertive anal sex. Symptoms and signs include pain in the scrotum, tenderness, and swelling of the scrotal contents with or without dysuria or urethral discharge. The testis is also often involved, resulting in epididymo-orchitis. Epididymitis must be distinguished from testicular torsion. Torsion generally will occur in younger men, 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

Patients usually present with unilateral scrotal pain and swelling with or without symptoms of urethritis; fever may be present. The pain and swelling may have a relatively sudden onset or be gradual. Sudden onset of unilateral pain and swelling in a young man should raise the suspicion of testicular torsion.

2. Examination

Patients with epididymitis will have scrotal swelling, tenderness, and possibly scrotal redness; the epididymis and often the testicle will be tender and swollen (the swelling usually begins at the tail, i.e., lower pole of the epididymis). Systemic symptoms such as fever may occur. It is very important to document that the epididymis is located posteriorly; an anterior epididymis with an elevated testicle suggests testicular torsion and requires immediate surgical evaluation. A negative cremasteric reflex is also concerning for testicular torsion. Note that epididymitis and testicular torsion can occur simultaneously. All cases of epididymitis should be presented to the attending physician.

3. Laboratory

Signs of urethritis (urethral discharge, positive urine leukocyte esterase test or ≥ 10 WBCs per high power field (40x) on spun urine) may be present. Urine-based gonorrhea and chlamydia NAAT tests should be done on all patients with epididymitis, as well as other STD screening as clinically indicated.

4. Diagnostic Criteria

Clinical symptoms and signs of epididymitis with or without signs of urethritis.

B. Treatment

- a. **Acute epididymitis in men who have sex with men (MSM);** i.e. differential diagnosis includes STDs and enteric organisms:
 1. **Ceftriaxone** 250 mg IM once *AND* **levofloxacin** 500 mg orally once daily for 10 days
- b. **Acute epididymitis in men aged < 35 years who have sex with women;** i.e. most likely caused by STDs:
 1. **Ceftriaxone** 250 mg IM once *AND* **doxycycline** 100 mg orally twice daily for 10 days
- c. **Acute epididymitis in men aged ≥ 35 years who have sex with women (or in non-sexually active men);** i.e. most likely caused by enteric organisms:
 1. **Levofloxacin** 500 mg orally once daily for 10 days *OR*
 2. **Ofloxacin** 300 mg orally twice a day for 10 days

Patients in whom a non-sexually transmitted etiology is suspected should be seen by the attending physician. Optimally, a urine culture is sent prior to treatment. Urologic consultation or follow-up may be indicated.

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

Indications for referral to ER:

- a. Significant fever *OR*
- b. Significant abdominal tenderness *OR*
- c. Toxic/acutely ill; extremely uncomfortable *OR*
- d. Rule out torsion (especially in young men with abrupt onset)

C. Follow-up

Patients should return for repeat evaluation in 5 days and demonstrate symptomatic improvement. Failure to improve within 5 days requires re-evaluation of the diagnosis or the therapy and consideration of urologic consultation. Swelling that persists unchanged for more than one month after beginning antimicrobial therapy should be evaluated for testicular cancer or other less common forms of epididymitis such as tuberculous 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 follow-up in five days.

4. Be counseled to notify partners from the past 60 days and refer them for examination and treatment.
5. Avoid sex for ≥ 10 days and until partner(s) are treated.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Be screened for HIV and other STDs according to current clinic guidelines.
8. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

Sex partners within the prior 60 days of patients with confirmed or suspected sexually transmitted acute epididymitis should be evaluated for STDs and empirically treated for chlamydial infections. Empiric treatment of partners for GC can be considered on a case by case basis.

Genital Herpes

Genital herpes is caused by one of two DNA viruses, herpes simplex virus (HSV) type 1 or type 2. It has an incubation period of 3 to 21 days, with an average of 6 days. Genital herpes is characterized by single or multiple vesicles anywhere on the genitalia, perineum or rectum. Vesicles rupture spontaneously to form shallow ulcers that are usually very painful. Because the vesicular phase may be missed, especially in women, ulcers may be the first sign. Lesions heal spontaneously, without scarring. The first occurrence, called "primary infection," has a mean duration of 12 days. Aseptic meningitis occurs infrequently during the first episode. In subsequent milder occurrences called "recurrent infections" lesions have a mean duration of five to ten days. Most anogenital herpes is caused by HSV-2, but an increasing proportion is attributed to HSV-1. Anogenital HSV-1 infections are less likely to recur than HSV-2 infections.

The interval between clinical episodes is called "latency". Although viral shedding is greatest during symptomatic periods, viral shedding occurs intermittently during latency and accounts for asymptomatic transmission. On the basis of serologic studies, the prevalence of HSV-2 infection has been estimated to be approximately 18% of the general sexually active population in the United States. Many persons with HSV anogenital infection have mild or asymptomatic disease and therefore have never been diagnosed and are not aware they have the infection.

Herpes zoster, which is a reactivation of varicella zoster (chickenpox) virus, is more common in immunocompromised individuals, and may be a sign of undiagnosed HIV-infection. Early in its course it may mimic HSV, but within hours or days it becomes more widespread as it develops its dermatomal (or generalized) pattern. The attending physician should be consulted in possible cases of disseminated (i.e. multidermatomal) zoster.

A. Diagnosis

1. History

- a. Patients may present with an initial episode of small blisters (vesicles) or with tender anogenital ulcers.
- b. Patients with a true primary infection (i.e. no prior history of either HSV-1 or HSV-2) have a more severe presentation, often with bilateral lesions, than those with prior clinical or serologic evidence of HSV-1.
- c. Patients may present with a history of recurrent anogenital lesions that may or may not be painful.
- d. A known history of contact to an infected partner is infrequent.

2. Examination

- a. Intact vesicles may be present and are strongly suggestive of HSV infection.
- b. The cervix may be involved, particularly in primary outbreaks, and can be erythematous, with shallow ulcers that may appear necrotic and friable.

- c. When herpetic ulcers become confluent, they may present as a large, painful solitary ulcer.
- d. Multiple shallow ulcers that mimic HSV may appear in patients with primary syphilis particularly in those who are HIV-infected.
- e. If ulcers and not vesicles are present then a complete evaluation of the anogenital ulcers must be done to distinguish between HSV, syphilis and chancroid (refer to the [genital ulcer protocol](#) for details).

3. Laboratory

- a. If vesicles are present, HSV infection is most likely. A swab for HSV PCR to assess the HSV type is useful to confirm the diagnosis and for counseling purposes. A VDRL or RPR should be sent, but additional evaluation of the vesicles is not necessary.
- b. For patients with a genital ulcer of unknown etiology, the full laboratory evaluation including HSV PCR as outlined in the [genital ulcer protocol](#) must be done.
- c. Type-specific HSV-2 antibody serologic testing should be considered in the following circumstances:
 1. To confirm a clinical diagnosis of herpes and to distinguish between primary and recurrent disease. HSV-2 PCR positive, HSV-2 antibody negative patients have primary infection whereas HSV-2 PCR positive, HSV-2 antibody positive patients may have long-standing infection, and may be either having a nonprimary first episode of herpes (if they do not recall ever having a herpes outbreak in the past), or a recurrence.
 2. Type-specific HSV-2 antibody testing can also be considered in patients with a partner with known genital HSV-2 infection to guide counseling and prevention messages.

4. Diagnostic Criteria

- a. The appearance of vesicular lesions anywhere in the anogenital region.
- b. Typical painful genital or anogenital lesion(s) and exclusion of other causes of genital ulcers.
- c. Recovery of HSV by PCR from vesicular fluid or scrapings of cervical, genital, or the anogenital lesions confirms the diagnosis.
- d. A positive type-specific antibody blood test signifies prior infection. However, HSV PCR is useful for confirming that the current symptoms are due to HSV.

B. Treatment

Oral anti-herpetic agents may be used episodically, to shorten the duration and severity of symptoms, or on an ongoing basis (i.e., suppressive therapy) to decrease frequency of recurrences and to decrease risk of transmission of HSV-2 to susceptible sex partners.

Topical antiviral therapy, though available, is less clinically beneficial than oral regimens and its use is discouraged.

Primary Episodes:

1. **Acyclovir** 400 mg orally three times daily for 7-10 days *OR*
2. **Famciclovir** 250 mg orally three times daily for 7-10 days *OR*
3. **Valacyclovir** 1 g orally twice daily for 7-10 days

*With all regimens, treatment may be extended beyond 10 days if lesions are not fully healed.

Episodic Recurrent Infection:

To be effective, episodic treatment should be initiated within 1 day of lesions or during the prodrome that may precede an outbreak.

HIV-uninfected:

1. **Acyclovir** 400 mg orally three times daily for 5 days *OR*
2. **Acyclovir** 800 mg orally twice daily for 5 days *OR*
3. **Acyclovir** 800 mg orally three times daily for 2 days *OR*
4. **Famciclovir** 1 g orally twice daily for 1 day *OR*
5. **Famciclovir** 500 mg once, then 250 mg twice daily for 2 days *OR*
6. **Valacyclovir** 1 g orally once daily for 5 days *OR*
7. **Valacyclovir** 500 mg orally twice daily for 3 days

HIV-infected:

1. **Acyclovir** 400 mg orally three times daily for 5-10 days *OR*
2. **Valacyclovir** 1 g orally twice daily for 5-10 days *OR*
3. **Famciclovir** 500 mg orally twice daily for 5-10 days

Daily Suppressive Therapy:

Suppressive therapy reduces the frequency of genital herpes recurrences by 70-80% among patients who have frequent recurrences. Patients who report marked anxiety/depression due to recurrent herpes may benefit from daily suppressive therapy. Suppressive therapy reduces the transmission of HSV infection from infected to uninfected partners.

HIV-uninfected:

1. **Acyclovir** 400 mg orally twice daily *OR*
2. **Valacyclovir** 1 g orally once daily *OR*
3. **Valacyclovir** 500 mg orally once daily*
*Valacyclovir 500 mg daily may not be effective suppression for people who experience frequent recurrences (i.e. 10 or more per year).

HIV-infected:

1. **Acyclovir** 400-800 mg orally 2-3 times daily *OR*
2. **Valacyclovir** 500 mg orally twice daily *OR*
3. **Famciclovir** 500 mg orally twice daily

C. Follow-up

Patients with an established diagnosis of HSV infection do not require follow-up. Patients in whom a presumptive diagnosis has been made during the initial evaluation of a genital ulcer should return in one week for a repeat evaluation (see [genital ulcer protocol](#)).

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Keep the lesions clean.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Be counseled about HSV transmission.
5. If pregnant, inform prenatal provider about the history of herpes.
6. Avoid sex while lesions are present.
7. Understand that a lesser, but real, risk of transmission exists during asymptomatic periods.
8. Be counseled about the potential benefits of suppressive therapy, including decreased risk of recurrences and decreased risk of transmission of HSV to sex partners.
9. Inform prospective sex partners of risk of exposure.
10. Refer sex partner(s) with lesions for evaluation.
11. Be offered condoms and advised that condoms can decrease risk of transmission.
12. Be screened for HIV and other STDs according to current clinic guidelines.
13. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation of Sex Partners

Sex partners of patients with HSV infection may benefit from counseling and evaluation including HSV serologic testing.

F. Special Considerations

Genital herpes infection during pregnancy

Acyclovir is pregnancy class B and available data suggest it is safe to use during pregnancy and lactation. Uncomplicated primary or recurrent genital herpes in pregnant women can be treated with oral acyclovir. Herpes can be transmitted to a neonate during delivery. The risk of perinatal transmission during a vaginal delivery in women with primary HSV infection is approximately 30-50%, whereas the risk is < 1% in women with a known history of herpes and vulvar recurrences at term. Because neonatal HSV infection is quite serious, most experts recommend that women with symptomatic HSV infections at the time of delivery should be delivered by cesarean section. Pregnant women with a known history of herpes, a new diagnosis of herpes infection during pregnancy, or with a partner with known or suspected herpes infection should inform their prenatal provider and be advised to discuss prevention of neonatal herpes. Pregnant women should be counseled that primary HSV-1 infection could occur through oral sex with a partner with orolabial herpes (cold sore).

Suppressive therapy should be considered beginning at 36 weeks gestation in women with a history of recurrent genital herpes. The recommended suppressive regimens for recurrent genital herpes in pregnancy are as follows:

1. **Acyclovir** 400 mg orally three times daily *OR*
2. **Valacyclovir** 500 mg orally twice daily

Genital Ulcer Disease

Anogenital ulcers result from several different sexually transmitted pathogens that may be difficult to distinguish clinically. In addition, more than one pathogen may be present. The most common clinical entities to consider include [herpes](#), [syphilis](#), and [chancroid](#). Other sexually transmitted infections that can present as anogenital ulcers include [lymphogranuloma venereum](#) (*Chlamydia trachomatis*, serovars L1, L2, L3), and granuloma inguinale (*Calymmatobacterium granulomatis*); which is rare in the United States and will not be addressed here. This protocol outlines the general evaluation of a patient with a anogenital ulcer. For specifics regarding the management of a patient with a anogenital ulcer for which the diagnosis has been established, refer to the protocol regarding the specific disease entity. The etiologic diagnosis of anogenital ulcer(s) by clinical presentation alone, even by experienced clinicians, is unreliable. Therefore, a thorough clinical and laboratory evaluation of all anogenital ulcers is extremely important.

One exception exists:

HSV lesions typically are small grouped lesions with vesicular/pustular centers and red borders. If vesicles are noted on exam, a diagnosis of HSV can be made. A serum VDRL or RPR should still be drawn, but further work up for diagnosis is unnecessary.

A. Diagnosis

1. History

The following characteristics should be ascertained during the history of present illness (HPI) when evaluating a patient with genital ulcer disease (GUD):

- a. Duration of ulcer(s).
- b. Date of last sexual contact (may help to identify etiologic agent by an obvious incubation period).
- c. Painful vs. painless.
- d. Was lesion a fluid-filled blister (vesicle) (e.g., HSV).
- e. Symptoms such as tingling/itching prior to appearance (e.g., HSV).
- f. History of ulcers in the past and similarity of previous ulcers to current ulcer(s); do they occur in same location (e.g., HSV).
- g. Any travel history or sex contacts in areas outside of the Bay Area (South East U.S., Africa, Central or South America, Caribbean, and Asia).
- h. Use of systemic or topical antimicrobial agents, or any new oral medications.
- i. Use of other topical preparations.
- j. Symptoms or signs in partner(s).

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 VDRL (or RPR). If the patient was treated for syphilis elsewhere, ask the patient if she/he knows the date of the last VDRL (or RPR) and whether or not it was reactive. Always attempt to obtain an accurate history regarding prior syphilis stage and treatment and document that information in the medical record.

2. Examination

Describe the following characteristics of the genital ulcer(s) and lymph nodes.

Ulcer(s):

- a. Number
- b. Location (Perianal ulcers not at 12 or 6 o'clock are particularly concerning for syphilis, as these are atypical locations for tears/fissures)
- c. Shape: oval, round, serpiginous, or rectangular
- d. Size
- e. Nature of the edges: raised, rolled, flat, or undermined
- f. Base of ulcer: purulent or clean
- g. Approximate depth of largest ulcer
- h. Tenderness
- i. Induration
- j. Friability
- k. Circumcision status

Lymph node(s):

- a. Number and location of enlarged nodes
- b. Size
- c. Tenderness
- d. Presence of bubo (if bubo is present, check for fluctuance – the attending physician should see any patients with a fluctuant bubo and drain it)
- e. Consistency: firm, rubbery, mobile, or soft

3. Laboratory

- a. Darkfield examination – If the initial darkfield examination is negative, it should be repeated (refer to [syphilis protocol](#) regarding technique).
- b. Swab for HSV PCR.
- c. HSV-2 type specific serology.

- d. Stat RPR, VDRL (or RPR) and clinician-ordered TPPA (Per lab protocol, the TPPA is not run if the non-treponemal antibody test (VDRL or RPR) is negative. The TPPA may be positive before the VDRL or RPR, so it is important to ask the lab to run the TPPA regardless of the VDRL or RPR result in suspected early cases).
- e. Stat TPPA (Syphilis Health Check™) may provide additional diagnostic information in patients with a genital ulcer when the DF is negative and the stat RPR is negative or weakly reactive. This test should only be used in patients who do not have a prior history of syphilis.

4. Diagnostic Criteria

- a. If the darkfield is positive then a diagnosis of primary syphilis can be made.
- b. If the stat RPR is reactive in the absence of a known serofast status, then a diagnosis of presumptive primary syphilis can be made (refer to [syphilis protocol](#)).
- c. If the Syphilis Health Check (stat TPPA) is positive in the absence of a known history of syphilis, then a diagnosis of presumptive primary syphilis can be made (refer to [syphilis protocol](#)).
- d. If the stat RPR and Syphilis Health Check (stat TPPA) are negative, consider a presumptive diagnosis of HSV and treat appropriately. In certain cases a clinician might still consider a primary syphilis diagnosis even with negative tests. In such cases it would be appropriate to treat for syphilis and HSV. If uncertainty remains, the attending physician should be consulted.

B. Treatment

1. In patients in whom syphilis is diagnosed or there is a high likelihood of syphilis, treat for primary syphilis (see [syphilis protocol](#)).
2. In pregnant women in whom syphilis cannot be ruled out, discuss with attending physician and consult syphilis treatment protocols. Penicillin is the only appropriate therapy for syphilis in pregnancy.
3. If herpes is suspected, treat for herpes as either initial or recurrent episode (see [HSV protocol](#)).

C. Follow-up

1. If herpes diagnosis is certain, no follow-up is necessary (refer to [HSV protocol](#)). Patients with anogenital ulcers of unclear etiology should return in one week.
2. At follow-up confirm medication adherence. If oral medication was prescribed, note any symptomatic improvement, verify that partner(s) have been treated, ask about a Jarisch-Herxheimer reaction (if the patient received an antimicrobial agent that has any activity against *T. pallidum*, regardless of whether or not the patient was presumptively diagnosed with syphilis), note any changes in the ulcer(s), and repeat the stat RPR and VDRL or RPR (if these tests were negative at initial visit). If the ulcer is not completely

healed, schedule a follow-up visit in one week. Continue to follow the patient until the lesion has healed completely.

D. Counseling/Education

Patients should:

1. Understand how to take the prescribed medication.
2. Know when to return for follow-up evaluation.
3. Avoid sex for at least 7 days until patient and partner(s) have been fully treated and the ulcers are totally healed.
4. Be screened for HIV and other STDs according to current clinic guidelines.
5. Be offered condoms and advised that condoms can prevent future infections.
6. Be counseled about PrEP if at elevated risk for HIV-infection. In addition, PrEP should be recommended to all patients with confirmed syphilis.

E. Evaluation and Treatment of Sex Partners

Sex partners of patients with genital ulcer disease must be evaluated. If a specific diagnosis has been made, refer to the appropriate protocol regarding which partners need to be referred. For genital ulcer disease of unknown etiology, partners within the past three months (90 days) should be evaluated.

F. Special Considerations

Reporting

Report suspected or confirmed syphilis cases to STD Control within 24 hours.

Genital Warts

Anogenital warts, or *condyloma acuminata*, are caused by human papillomavirus (HPV), the most common sexually transmitted infection in the US. 90% of anogenital warts are caused by HPV strains 6 or 11. HPV has a variable incubation period, which averages two to six months, but may be much longer. Patients who develop warts due to HPV may have single or multiple soft, fleshy growths anywhere around the anogenital region, which are usually painless, but can be painful, friable, or pruritic depending on the lesion size and/or location. The warts may have a flat morphology, which can be very difficult to detect. Clinically, anogenital warts should be distinguished from other papular and warty lesions including pearly penile papules, skin tags, *condyloma lata* of secondary syphilis and molluscum contagiosum. Biopsy is necessary for pigmented or atypical external warts to rule out malignancy.

A. Diagnosis

1. History

- a. Patients may present with painless anogenital “bumps” or lesions that may have been present for many weeks; continued growth of the long-standing lesions is not uncommon. Women with vulvar warts and individuals with perianal or rectal warts may have itching.
- b. Many patients present with recurrent warts.
- c. Known exposure to a partner with anogenital warts is infrequent. Exposure to a partner with a history of warts does not necessarily mean that the patient will develop visible warts in the future.

2. Examination

- a. Warts may be found on any part of the genitalia, perianal area, in the anal canal and rectum, and in the inguinal area.
- b. They usually have a characteristic raised or flat fleshy appearance and range between 1-5 mm although warts that have been present for a long time may be larger and keratotic. Grouped warts may attain a size of several centimeters.
- c. Care must be used not to mistake *condyloma lata*, a flat skin manifestation of secondary syphilis, for *condyloma acuminata*. Pearly penile papules and Tyson’s glands in men, as well as vaginal papillae in women, may also mimic warts.

3. Laboratory

- a. HPV DNA typing has no role in the routine clinical evaluation of anogenital warts.
- b. If there is any clinical suspicion for syphilis, obtain a specimen from the lesion for darkfield microscopy and perform a stat RPR and lab based non-treponemal antibody test (VDRL or RPR).
- c. Obtain other STD screening as indicated.

4. Diagnostic Criteria

- a. Diagnosis is clinical and based on visual inspection of lesions.
- b. Any atypical or deeply pigmented lesions on the genitals, perianal area, or rectum should be referred for biopsy.
- c. Lesions that do not respond to standard therapy or worsen during therapy should be referred for biopsy.
- d. Possible *condyloma lata* should be evaluated by darkfield microscopy, stat RPR and VDRL (or RPR).

B. Treatment

Warts are treated for cosmetic purposes and symptom management (e.g., bleeding, discomfort with sex), and warts that are left untreated may remain unchanged, grow in number and size, or regress spontaneously. While patients may experience psychological morbidity from the presence of anogenital warts, there are no clear medical indications supporting routine therapy. Treatment of anogenital warts reduces the amount of HPV viral DNA present, but whether this reduces future transmission is unclear. There is no evidence that the presence of anogenital warts or their treatment is associated with the development of cervical or anal cancer.

There is no clear evidence that one treatment option is superior to the others. Treatment is divided into provider vs. patient-administered therapies, and should be chosen based on patient preference, availability of resources, and provider experience.

Provider-Administered Therapies:

1. **Liquid nitrogen (LN2)** can be applied topically with a swab. The swab should be left on the wart(s) for a slow 10 second count, the wart should be allowed to thaw, and then the treatment should be repeated for up to three cycles. The freeze/thaw cycle results in cell cytolysis which destroys the wart. Side effects include discomfort up to 15 minutes after the procedure, erythema and possible blistering at treatment site. Multiple treatments at three-week intervals are usually required.
2. **Podophyllin 25%** can be applied topically with a swab. It is a plant extract that inhibits cell division. The podophyllin must dry completely so that normal skin does not come into contact with the medication, and patients must be instructed to wash the podophyllin off one to four hours after it has been applied. Podophyllin should not be applied to areas that are occluded such as under the foreskin or to mucous membranes, open lesions, wounds or friable tissue. Podophyllin has the potential to be neurotoxic, oncogenic, teratogenic and mutagenic and so should not be used in pregnancy or to treat extensive warts with a large surface area. Side effects may include erythema, ulceration or pain at treatment site within 48 hours after application.
3. **Trichloroacetic acid (TCA)** in alcohol is useful for warts on mucous membranes. It can be applied with the end of a cotton swab. Extreme care must be used when applying it

to prevent burns. Avoid all contact with normal skin around wart. Area must be allowed to dry (i.e., develop a white frost on the tissue) before patient sits or stands. TCA causes a chemical coagulation of cell proteins, which destroys the wart. Side effects include pain, erythema, burning, and ulceration. If pain is bothersome, patient can neutralize acid by applying baking soda or talcum powder to treated area or washing area with liquid soap. Treatment can be applied weekly if necessary.

4. **Electrocautery, surgical excision.** For severe disease – requires referral to appropriate specialist.

Patient-Applied Therapies:

1. **Podofilox 0.5%** solution (3.5 ml) or gel (3.5 g) is applied with a cotton swab or finger to visible warts twice daily for three consecutive days followed by four days without treatment. This cycle can be repeated as necessary for a total of four times. Total wart area treated should not exceed 10 cm² and total volume limited to 0.5 mL per day. Similar to podophyllin, podofilox prevents cell division. However, it is more stable than podophyllin and therefore safe for patient administration. Side effects may include erythema, swelling, and erosions at the treatment site. Podofilox is available only by prescription (\$100.00/3.5 ml solution at Walgreens as of March 2016) and is covered by Family PACT. Should not be used in pregnancy.
2. **Imiquimod 5% or 3.75%** cream (distributed in small packets). Imiquimod 5% cream is applied with fingertip at bedtime three times a week for up to sixteen weeks. Imiquimod 3.75% cream is applied with fingertip at bedtime each night for eight weeks. Wash off with a mild soap and water 6-10 hours after each application. Imiquimod does not have direct antiviral properties, but stimulates the local immune response. Some studies indicate it has a lower recurrence rate than other wart treatment. Side effects may include local erythema, ulceration, and hypopigmentation. Imiquimod is available only by prescription (\$320/one month treatment at Walgreens as of March 2016) and is covered by Family PACT. Should not be used in pregnancy.
3. **Sinecatechins 15%** ointment is applied as a 0.5 cm strand of ointment to each wart three times daily using a finger to ensure coverage with a thin layer of ointment until complete clearance of warts for a maximum of sixteen weeks. Do not wash off. Avoid sexual contact, may also weaken latex barriers. Side effects can include erythema, pruritis/burning, pain, ulceration, edema, induration and vesicular rash. Sinecatechins are a green tea extract with an active product (catechin) that inhibits specific HPV gene products. This product is not recommended for individuals with HIV infection, other immunocompromising conditions or genital herpes. Safety of use during pregnancy is unknown.

If internal anal warts are noted on routine visual anal inspection and patient requests treatment, referrals can be made (for San Francisco residents) to the general surgery clinic at Zuckerberg San Francisco General (ZSFG). Referrals should be placed through e-referral or by calling (415) 206-8673. If extensive vaginal warts are noted on exam and patient

requests treatment, referrals can be made (for San Francisco residents) to the Women's Clinic at ZSFG where the patient will be evaluated and possibly referred for surgery.

C. Follow-up

Patients being treated with LN2, TCA and podophyllin 25% should return at three-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.

D. Counseling/Education

Patients should:

1. Be counseled about external anogenital warts and HPV and be told that:
 - a. Genital HPV infection is very common. Most sexually active adults will get HPV at some point, but in most cases it is asymptomatic and clears spontaneously.
 - b. The types of HPV that cause anogenital warts are different from the types that can cause anogenital cancers.
 - c. A diagnosis of HPV in one sex partner is not indicative of sexual infidelity in the other partner.
2. Return for provider-applied treatment every three weeks until lesions have disappeared, if needed/desired.
3. Understand that after treatment of visible warts, the potential for transmission may persist and that recurrences are very common.
4. Be offered condoms and advised that condom use is associated with faster rates of regression of cervical intraepithelial neoplasia, penile warts in men, and the clearance of cervical HPV infection in women.
5. Be advised that consistent condom use has been shown to decrease the acquisition of HPV and incidence of external anogenital warts in men and reduce HPV acquisition in women, but that condoms are not fully protective because HPV can infect areas not covered by a condom.
6. Be informed that women should get regular [pap smears](#) as recommended, regardless of genital wart history, to screen for precancerous lesions associated with HPV.
7. Be offered HPV vaccination if never immunized and meets age-based criteria (see [HPV](#)) – warts are not a contraindication to HPV vaccination.
8. Be screened for HIV and other STDs according to current clinic guidelines.
9. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

Current sex partners of patients with HPV infection can be examined for anogenital warts and, if present, may be treated with an appropriate regimen for warts. Acetoacetic acid (vinegar) should not be used to detect genital warts, as the whitening that occurs is very nonspecific. HPV testing is not indicated. Partners should also be screened for other STDs as indicated and female partners have a Pap smear if indicated by screening guidelines.

F. Special Considerations

Genital warts in pregnancy

Podophyllin, podofilox, imiquimod and sinectechins are not approved for use during pregnancy. Pregnant women can be treated for warts with LN2 or TCA. Although genital warts may be transmitted to infants during delivery, the risk is thought to be quite low and cesarean delivery is not indicated in pregnant women with warts.

Colposcopy

Colposcopy services are available to eligible City Clinic patients through the family planning clinic. Consult the family planning clinicians for further details. Patients with expophytic cervical warts should have a biopsy to exclude high-grade squamous intraepithelial lesions (SIL) before treatment is initiated.

Gonorrhea

The Gram-negative bacterium *Neisseria gonorrhoeae* (GC) can infect the urethra, cervix, rectum, pharynx, and in rare cases may become disseminated (bloodborne). Infections caused by antimicrobial-resistant *N. gonorrhoeae* are clinically indistinguishable from those caused by antimicrobial-susceptible strains. Sexually transmitted infections caused by GC may be symptomatic or asymptomatic. Urethral GC in men is usually symptomatic and is characterized by the acute onset of purulent urethral discharge, often accompanied by pain with urination that begins approximately 1-10 days (average 2-5 days) after exposure. Women with cervicovaginal GC may have abnormal vaginal discharge, abnormal bleeding, pelvic pain or pain with urination, but as many as 50-70% of women with GC are asymptomatic. In addition, the majority of gonococcal infections in the rectum and pharynx are asymptomatic. Serious complications of gonococcal infection include pelvic inflammatory disease with subsequent infertility or risk of ectopic pregnancy in women, and epididymitis and urethral stricture in men. Disseminated gonococcal infection (DGI) may occur in either sex, 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 gonococcal eye infection (*ophthalmia neonatorum*), scalp abscess at the site of fetal monitors, and disseminated infections.

A. Diagnosis

1. History

Symptoms will vary depending on the site of infection. GC infections in both men and women can be asymptomatic. Women with a positive GC test from a cervical, vaginal or urine specimen who have suggestive symptoms should be evaluated for pelvic inflammatory disease.

- a. Cervix –Vaginal discharge, lower abdominal pain, pain with intercourse, post coital bleeding or pain with urination.
- b. Urethra –Pain with urination, discharge.
- c. Rectum –Discharge (usually described as mucous on stools), tenesmus, perianal itching, rectal pain and possibly rectal bleeding.
- d. Pharynx – Usually asymptomatic, or patients may complain of a sore throat or pain with swallowing.
- e. DGI – see section F below.

2. Examination

Signs of infection may or may not be present.

- a. Cervix – mucopurulent or frankly purulent cervical discharge, redness, and friability.
- b. Urethra – purulent discharge, possibly phimosis and swelling, tender inguinal adenopathy.
- c. Rectum – purulent exudate (clinicians should use anoscope for proper rectal examination).
- d. Pharynx – rarely redness, exudate (most have no signs of infection and when present are nonspecific).
- e. DGI – see [section F](#) below.

3. Laboratory

- a. A Gram stain of the discharge should be done and the discharge should be streaked on a modified Thayer-Martin (MTM) plate for GC culture.
- b. A nucleic acid amplification test (NAAT) is the preferred screening test for genital gonorrhea infection and can be performed from urine, vaginal, urethral or cervical samples. In women, a self-collected or provider-collected vaginal swab is the specimen of choice. A urine specimen can be tested if there is a tampon in place or the patient is unwilling or unable to have a vaginal swab collected. Labs that have met CLIA requirements and validated gonorrhea NAAT testing from extragenital sites can perform a gonorrhea NAAT test on an oropharyngeal or rectal sample. Pharyngeal screening is recommended for men who report oral receptive sex (i.e., performed fellatio) and rectal screening is recommended for men who report receptive anal sex. See current clinic guidelines for specific recommendations regarding indications for pharyngeal and rectal chlamydia screening.

4. Diagnostic Criteria

- a. Isolation of *N. gonorrhoeae* from sites of exposure (e.g., urethra, pharynx, endocervix, rectum) by culture or NAAT.
- b. Gram stain should be performed to evaluate all discharges. The sensitivity of Gram stain of urethral discharge in men is near 95%. The endocervical Gram stain has a sensitivity of approximately 50%, and a specificity of 95%. In persons attending City Clinic who have a Gram stain showing Gram-negative intracellular diplococci, there is a high positive predictive value and such persons should be treated for GC. Gram stain of the oropharynx is not advised because of the plethora of other pharyngeal bacteria of the *Neisseria* family that will stain similarly to *N. gonorrhoeae*.

B. Treatment

a. Uncomplicated Cervicovaginal, Urethral or Rectal Infection

Due to the threat of future emergence of cephalosporin resistance, patients with GC or suspected GC should receive *dual therapy* with two antibiotics, administered at the same time, regardless of chlamydia test result. In 2015, CDC revised its gonorrhea treatment guidelines to make ceftriaxone, administered with azithromycin, the sole recommended regimen for uncomplicated GC. The CDC no longer lists cefixime-based dual therapy as a recommended treatment regimen for gonorrhea; this has been moved down to an alternative regimen. In addition, dual therapy with doxycycline is no longer recommended because of the advantages of single-dose therapy offered by azithromycin, and the substantially higher prevalence of GC resistance to tetracycline than to azithromycin. If the patient has been treated with at least 1 g of azithromycin in the past 5 days, the azithromycin dose does *not* need to be repeated at the time of ceftriaxone administration.

Recommended regimen:

1. **Ceftriaxone** 250 mg IM in a single dose once and **azithromycin** 1 g orally once

Alternative regimen:

1. **Cefixime** 400 mg orally once and **azithromycin** 1 g orally once

b. Uncomplicated Pharyngeal Infection

1. **Ceftriaxone** 250 mg IM in a single dose once and **azithromycin** 1 g orally once

Note: Oral antibiotics alone should not be used to treat pharyngeal GC infection due to poor antibiotic penetration into the oropharynx.

c. Alternative Regimen for Patients with Allergy

Should be reserved for individuals with severe penicillin or cephalosporin allergy (defined as hives, angioedema, anaphylaxis or Stevens Johnson Syndrome/toxic epidermal necrolysis):

1. **Gentamicin** 240 mg IM in a single dose once and **azithromycin** 2 g* orally once *OR*
2. **Gemifloxacin** 320 mg orally once and **azithromycin** 2 g* orally once

**Note: Warn patients about possible gastrointestinal side effects when administering 2 g azithromycin*

d. Treatment of DGI

See [section F](#) below and call for expert consultation: (415) 487-5595.

C. Follow-up

1. Test of cure is NOT required for persons with uncomplicated urogenital or rectal GC who are treated with any of the recommended or alternative regimens.
2. Persons with pharyngeal GC who are treated with an alternative regimen should return 14 days after treatment for a test of cure using either culture or NAAT. If the NAAT is positive, effort should be made to perform a confirmatory culture before retreatment. Positive cultures from a test of cure should undergo antimicrobial susceptibility testing.
3. Symptoms that persist after treatment should be evaluated with a GC culture.
4. All patients should return for repeat testing for GC **three months** after treatment because re-infection is common.
5. Suspected Cephalosporin Treatment Failure

Symptoms that persist after treatment are more likely due to re-infection rather than treatment failure. Patients should be questioned regarding the possibility of re-infection, including any new sex partners or repeated exposure to an untreated partner.

If the patient does not give a history of interval sex, and treatment failure is suspected, obtain a culture for *N. gonorrhoeae*. Positive culture should undergo antimicrobial susceptibility testing. Consult with the attending physician for current clinic protocols for evaluation and management of suspected GC treatment failure.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Be counseled to notify sex partners from the past 60 days and refer them for evaluation and treatment, or provide them with patient-delivered partner therapy if partners are unlikely to present to care (see [section E](#)).
4. Avoid sex for at least 7 days and until partner(s) have completed therapy.
5. Be advised to return in 3 months for repeat testing to rule out re-infection.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Be tested for HIV and syphilis, and screened for other STDs according to current clinic protocols.
8. Understand the importance of regular screening (if MSM or age ≤ 25 years) since gonorrhea in women, and rectal/pharyngeal gonorrhea in men, is often asymptomatic.

9. Be counseled about PrEP if at elevated risk for HIV-infection (note that PrEP should be recommended to MSM, trans women and trans men who are HIV-negative and have rectal gonorrhea).

E. Evaluation and Treatment of Sex Partners

All sex partners in the prior 60 days of patients who have been diagnosed with *N. gonorrhoeae* infection should be examined, tested, and empirically treated for *N. gonorrhoeae* and *C. trachomatis*.

Patient-delivered partner therapy (PDPT) with cefixime 400 mg orally once and azithromycin 1 g orally once can be offered to patients with GC, particularly if they report that it is unlikely that their partners will present to a clinic for evaluation. Patients should inform their partners that it is optimal for them to come to a clinic to receive an injection of ceftriaxone (in addition to oral azithromycin), and be screened for other STDs including HIV, but that if this is not feasible, they should take the patient-delivered partner therapy instead. Men should be strongly encouraged to refer female partners for clinician evaluation.

F. Special Considerations

Disseminated Gonococcal Infections (DGI)

Although uncommon, *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 fever, pustular skin lesions, erythema and swelling of a joint (often a single joint), and/or tenosynovitis – redness, swollen or tender tendon sheath(s). Patients with suspected DGI should be evaluated by the attending physician.

Recommended therapy for DGI includes 7 days of anti-gonococcal antibiotics. Consider hospitalization for severe disease. Patients should be treated with ceftriaxone 1 g IM or IV every 24 hours (plus azithromycin 1 g orally in a single dose) and should be evaluated daily to assess for clinical improvement. This regimen should be continued for 24-48 hours after clinical improvement begins, at which time therapy can be switched to cefixime 400 mg orally twice daily to complete the remainder of the seven-day course.

Reporting

Report confirmed or suspected gonorrhea cases to STD Control within 1 week.

Hepatitis A and B

Vaccine Preventable STDs

One of the most effective methods to prevent the acquisition of STDs is pre-exposure immunization. Currently licensed vaccines for the prevention of STDs include those for hepatitis A, hepatitis B and [HPV](#). In addition, the quadrivalent meningococcal vaccine is recommended for all HIV-infected individuals and in San Francisco, it is also recommended for all MSM and trans women who have sex with men. City Clinic is currently offering the hepatitis A, hepatitis B, HPV, and meningococcal vaccine series to eligible patients. Refer to current clinic guidelines regarding vaccine availability.

Hepatitis A

Hepatitis A is caused by infection with the hepatitis A virus (HAV). HAV replicates in the liver and is shed in the feces. Virus in the stool is found in the highest concentrations from two to three weeks before to one week after the onset of clinical illness. Virus is also present in serum and saliva during this period, although in much lower concentrations than in feces. The most common mode of HAV transmission is fecal-oral: either person-to-person transmission between household contacts or sex partners, or by contaminated food or water. Transmission between sex partners occurs because of oral-anal contact. Because viremia occurs in acute infection, bloodborne HAV transmission can occur, but it has been reported infrequently. Although HAV is present in low concentrations in the saliva of infected persons, saliva has not been demonstrated to play a role in transmission.

Up to 20% of persons with acute hepatitis A require hospitalization and 0.1% will develop fulminant liver failure. The overall mortality rate for acute hepatitis A is 0.5%, but is higher (1.8%) in adults over 49 years and one study suggested among those with chronic hepatitis C mortality may be as high as 40%. HAV infection is not associated with chronic liver disease.

Outbreaks of hepatitis A among men who have sex with men have been reported in urban areas, both in the U.S. and abroad. The prevalence of HAV infection among men who have sex with men has been found to be significantly higher than that among heterosexual men (30% vs. 12%) in one study.

A. Pre-exposure Prophylaxis

Pre-exposure protection against HAV infection by immunization with hepatitis A vaccine is indicated for the following risk groups:

1. Sexually active men who have sex with men
2. Persons who have used illicit drugs (injection and non-injection) in the past year
3. Persons with chronic liver disease, including chronic hepatitis C (HCV)
4. Travelers to endemic areas (refer these clients to the SF Department of Public Health Adult Immunization and Travel Clinic at 101 Grove)

5. In addition, adults who seek protection from Hepatitis A virus infection may receive the vaccine; acknowledgement of a specific risk factor by those who seek protection is not needed.

B. Dosing

Adults – **Havrix** (1440 EL.U) or **Vaqta** (50 units) hepatitis A vaccine IM at 0 and 6 months. If using combined Hepatitis A and B vaccine (Twinrix), doses are given at 0, 1 and 6 months. No need to repeat or restart if doses are late.

C. Post-exposure Prophylaxis

High-risk non-immune patients exposed to a person with acute HAV (household, sexual or IDU contact) should receive either single-antigen HAV vaccine or intramuscular HAV immune globulin (IG) as soon as possible, ideally within 2 weeks of exposure. Vaccine is preferred for healthy people ages 12 months to 40 years. The following people should receive IG instead of HAV vaccine for PEP: immunocompromised people (including those with HIV/AIDS), those undergoing hemodialysis, transplant patients, patients on high dose steroids and those with contraindications to the vaccine. Patients who receive IG and do not have contraindications to the vaccine should also begin the HAV vaccination series (at a separate injection site) as outlined above.

Hepatitis B

Sexual transmission accounts for an estimated 30-60% of the estimated 75,000 new HBV infections that occur annually in the United States. Of persons infected as adults, 6-10% develop chronic HBV infection. These persons are capable of transmitting HBV to others and are at risk for developing chronic liver disease and liver cancer. HBV infection leads to an estimated 5,000 deaths annually in the United States from cirrhosis of the liver and primary liver cancer.

A. Pre-exposure Prophylaxis

With the implementation of routine infant hepatitis B immunization in 1991 and the wide scale implementation of programs to vaccinate adolescents, immunization of high-risk adults has become a high priority in the strategy to eliminate HBV transmission in the United States. All persons attending STD clinics, or persons known to be at high-risk for acquiring HBV infection (e.g., persons with multiple sex partners, sex partners of persons with chronic HBV infection, or injection-drug users) should be advised of their risk for HBV infection and offered hepatitis B immunization.

B. Screening for Antibody or Immunizing without Screening

The prevalence of past HBV infection among sexually active men who have sex with men and among injecting-drug users is high. Although serologic screening for evidence of past infection before vaccinating adults ≥ 30 years of age may be cost-effective in a primary care setting, at City Clinic we vaccinate patients born before 1991 who are unsure of their HBV status without screening for antibodies. At the current cost of vaccine, it is not cost-

effective to perform pre-vaccination testing on adolescents or young adults. Vaccination of a person who is already immune is not harmful.

C. Dosing

Adults/Adolescents – **Recombivax HB** (10 mcg) or **Engerix-B** (20 mcg) hepatitis B (IM) at 0, 1, and 4 months. No need to restart or repeat doses if missed or late.

D. Post-exposure Prophylaxis

Exposure to an HBsAg-Positive Source (i.e. a person with chronic, active HBV)

Unvaccinated persons, incompletely vaccinated or persons known not to have responded to a complete hepatitis B vaccine series should receive both HBIG and hepatitis vaccine as soon as possible (preferably ≤ 24 hours) after an identifiable exposure to blood or body fluids that contain blood from a person with HBV. HBIG is unlikely to be effective if given > 7 days after the exposure. Patients should be referred to urgent care or an ER for HBIG. If the source is tested and turns out to be HBsAg negative, the exposed person should still complete a HBV vaccine series.

Individuals who have been vaccinated, but who did not have post-vaccination testing and/or do not know if they have protective antibodies to HBV (i.e. HBsAb positive), should receive a single vaccine booster dose.

Exposure to Persons with Unknown HBsAg Status

Unvaccinated persons who have a discrete, identifiable exposure to blood or body fluids from a source with unknown HBsAg status should receive the hepatitis B vaccine series as soon as possible after exposure (preferably within 24 hours).

E. Special Considerations

Pregnancy

Pregnancy is not a contraindication to hepatitis B vaccine or HBIG administration.

Human Papillomavirus (HPV): Prevention and Screening

There are more than 100 types of HPV, over 40 of which can infect the genital area. Oncogenic, or high-risk HPV types (e.g., HPV types 16 and 18) cause cervical and anal cancers and precancers, while nononcogenic, or low-risk HPV types cause [anogenital warts](#) and recurrent respiratory papillomatosis. Oncogenic HPV types are also associated with penile, vulvar and vaginal cancer, as well as some oropharyngeal cancers.

A. Primary Prevention of HPV (vaccines)

Three HPV vaccines are available in the United States: a bivalent vaccine (Cervarix) prevents infection with HPV types 16 and 18, a quadrivalent vaccine (Gardasil-4) prevents infection with HPV types 6, 11, 16 and 18, and a 9-valent vaccine (Gardasil-9) prevents infection with HPV types 6, 11, 16, 18, 31, 35, 45, 52, and 58. All three vaccines offer protection against HPV types 16 and 18, which account for 66% of all cervical cancers; the quadrivalent and 9-valent HPV vaccines protect against types 6 and 11 which cause 90% of anogenital warts; and the 9-valent vaccine protects against five additional HPV types that account for 15% of cervical cancers.

Cervarix is indicated for the prevention of cervical cancer in women. Gardasil-4 and gardasil-9 are indicated for the prevention of cervical cancer, anal cancer, and genital warts and both are approved for use in males and females aged 9-26 years. HPV vaccines are administered as a 3-dose series over a 6-month period with the second and third doses administered 1-2 and 6 months after the first dose, respectively. Women who have received HPV vaccine should continue routine cervical cancer screening (i.e., with Pap smears) if they are ≥ 21 years. The benefit of the vaccine is greatest if administered prior to the onset of sexual activity, however HPV vaccines can be administered regardless of history of anogenital warts, abnormal Pap/HPV tests or anogenital precancer. HPV vaccines are not recommended for use in pregnant women.

Gardasil-9 is available at City Clinic for eligible males and females up to age 26. Refer to current clinic guidelines for details regarding vaccine eligibility and availability.

B. Cervical Cancer Screening (Pap smears)

The Papanicolaou (Pap) smear is an effective and relatively low-cost screening test for invasive cervical cancer and squamous intraepithelial lesions (SIL), the precursors of cervical cancer. Women attending STD clinics are at increased risk for cervical cancer. Prevalence studies have found that precursor lesions for cervical cancer occur about five times more commonly among women attending STD clinics than among women attending family planning clinics. Moreover, studies conducted among women attending STD clinics indicate that many women do not understand the importance of Pap smears and almost half of women who have had a pelvic examination erroneously believe they had a Pap smear when they actually have not.

Because MSM, particularly HIV-infected MSM, are at increased risk for anal HPV infection and anal cancer, some clinics offer anal Pap smear screening to men at high-risk for this infection. However, data are limited on the natural history of anal intraepithelial neoplasia (AIN) and the safety and response to the treatment of AIN, and the personal and public health benefit of anal Pap screening is unknown. Clinics offering anal Pap smears should have access to high resolution anoscopy (HRA) to follow-up abnormal cytologic findings identified on anal Pap screening.

1. Recommendations

The American College of Obstetricians and Gynecologists (ACOG) screening guidelines recommend the following for HIV-negative women with no history of an abnormal pap smear:

1. Age < 21: Cervical cancer screening should be avoided.
2. Age 21-30: Pap test every 3 years.
3. Age ≥ 30-65: Pap test every 3 years OR Co-testing (Pap test and HPV testing) every five years if both initial tests are negative (note that HPV testing not currently available at SF City Clinic)

2. Counseling and Education

At the time of a pelvic examination for STD screening, the health care provider should inquire about the result of her last Pap smear and should discuss the following information with the patient:

1. Purpose and importance of a Pap smear.
2. Whether a Pap smear was obtained during the clinic visit.
3. Offer to perform a Pap smear at the visit if it has been more than 3 years since last done, or if the patient has missed a follow-up for a previously abnormal Pap.
4. Women “out of the care loop”, psychiatric patients, and homeless women should have a Pap done on an STD visit while there is an opportunity to do it. It is important not to miss opportunities to perform Pap smears in these patients when they present to STD clinic.
5. Note that as of February 2017, at City Clinic we are only able to offer pap smears to women who have Family PACT or who are uninsured, San Francisco residents.

3. Other Management Considerations

Other considerations in performing Pap smears are the following:

1. The presence of a mucopurulent discharge should not delay the Pap smear. A Pap smear can be obtained after gentle removal of the discharge with a saline-soaked cotton swab (Scopette).
2. Liquid-based cytology can be performed during menstruation. Conventional cytology Pap test should be postponed if a woman is menstruating.

3. A woman with external genital warts does not need to have Pap smears more frequently than a woman without warts, unless otherwise indicated.
4. Women who have had hysterectomies do not require annual Pap smears unless the hysterectomy was related to cervical cancer or its precursor lesions, or if the woman is HIV-infected. If screening is indicated, the patient should be advised to continue follow-up with the physician(s) involved in their care at that time for vaginal cytologic screening.

A. Colposcopy

City Clinic provides colposcopy to women who have Family PACT or who are uninsured, San Francisco residents.

B. Special Considerations

Pregnancy

Women who are pregnant should have a Pap smear as part of routine prenatal care. A cytobrush may be used for obtaining Pap smears in pregnant women, although care should be taken not to disrupt the mucous plug.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is a sexually transmitted disease caused by serovars (subtypes) L1, L2, or L3 of *Chlamydia trachomatis*. LGV can be asymptomatic, or it can present in a variety of clinical syndromes, most commonly characterized by proctitis/proctocolitis or the bubonic form with tender inguinal lymphadenopathy. Unlike mucosal infections caused by non-LGV serovars of *Chlamydia trachomatis*, LGV can induce a lymphoproliferative reaction and can be an invasive, systemic disease.

A. Diagnosis

1. History

- a. The clinical presentation of LGV can vary and the incubation period is 3 to 12 days or longer.
- b. 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, patients are rarely identified at this stage. Untreated infection extends to lymph nodes and 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 after 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.
- c. The proctitis syndrome, the presentation most commonly seen in MSM, is characterized by rectal discharge, bleeding, ulcerative proctitis and painful inflammation progressing to proctocolitis. LGV proctitis has been associated with HIV acquisition and sexually transmitted hepatitis C virus (HCV) infection in MSM. Rare complications of LGV include chronic inflammation with development of genital elephantiasis, fistulas, and rectal strictures, sometimes requiring surgical intervention.
- d. LGV should be considered in MSM and trans women who have sex with men who present with rectal complaints or a tender lymphadenopathy syndrome.

2. Examination

- a. Patients may present with a papule, ulcer, erosion or small herpetiform lesion on the genitals. The primary lesion of LGV is usually asymptomatic and heals rapidly on its own, so patients rarely present at this stage of infection.
- b. Painful, fluctuant inguinal lymphadenopathy, usually unilateral, may be present.
- c. The most common presentation is bloody, purulent or ulcerative proctitis, though rectal LGV infection can be asymptomatic.

- d. Chronic, untreated LGV can lead to perirectal abscesses, anal fistulas or rectal strictures.

3. Laboratory and Diagnostic Criteria

- a. Currently, there is no commercially available test for LGV and in most settings, the diagnosis should be considered based on a compatible clinical presentation.
- b. NAATs are very sensitive for chlamydia but do not distinguish between LGV and non-LGV serovars. The chlamydia culture, though not as sensitive as the NAAT, may be DNA sequenced to identify LGV serovars; however, chlamydia culture is not widely available. LGV serology is not helpful for diagnosis.
- c. The SFDPH Public Health Lab (PHL) has validated a PCR assay for LGV from rectal swabs. If testing is to be performed at the PHL, an additional swab should be collected and sent in viral transport media for LGV testing. The LGV PCR will be run only if the rectal CT NAAT is positive. This test is batched, and providers should initiate empiric treatment for LGV rather than wait for the results of the LGV PCR.
- d. In patients with proctitis (see [proctitis](#)), providers should collect specimens to test for chlamydia (rectal swab and urine sample for chlamydia NAAT) and presumptive treatment for LGV should be considered, particularly if the patient has bloody discharge or mucosal ulcers.
- e. *Consult the attending physician for any cases of suspected LGV.*

B. Treatment*

1. **Doxycycline** 100 mg orally twice daily for 21 days

Alternate:

1. **Azithromycin** 1 g orally qweek x 3 weeks may be effective, but clinical data are limited,
OR
2. **Erythromycin** 500 mg orally four times daily for 21 days

*Consider dispensing 7 days and asking the patient to follow-up in one week. If the rectal CT NAAT is negative, then LGV has been ruled-out and no additional treatment is needed. However, if the clinical suspicion for LGV is high and/or it is unlikely that the patient will return to clinic, the full 21 day course should be dispensed

C. Follow-up

The patient should return to clinic in one week. If the initial rectal CT NAAT is negative, doxycycline can be discontinued after a 7-day course is completed. If the rectal CT NAAT is positive, doxycycline should be continued for the full 3 weeks. The LGV-specific test result may not be available for several weeks.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refer sex partners from the past 60 days for examination and treatment. Patients should be offered patient- delivered partner therapy if their partners are unlikely to present to clinic for examination and treatment.
4. Avoid sex for at least 7 days until both they and their partner(s) are fully treated, and symptoms have resolved.
5. Be advised to return in 3 months for repeat testing to rule-out re-infection.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Be tested for HIV and syphilis, and screened for other STDs according to current clinic protocols.
8. Be counseled about PrEP if at elevated risk for HIV-infection. In addition, PrEP should be recommended to all HIV-negative patients with confirmed LGV.

E. Evaluation and Treatment of Sex Partners

Optimum treatment for partners of patients with LGV is not known; at City Clinic, partners are treated with standard regimens for uncomplicated chlamydia infection:

1. **Doxycycline** 100 mg twice daily x 7 days *OR*
2. **Azithromycin** 1 g orally once

Partners should be encouraged to come to clinic for evaluation, particularly if they develop symptoms of proctitis (rectal discharge, irritation) or inguinal lymphadenopathy.

Molluscum Contagiosum

Molluscum contagiosum, caused by a poxvirus, is characterized by smooth, spherical papules with umbilicated centers that can occur anywhere on the body except the palms and soles. When found on the skin of the genitalia, the thighs, and the lower abdominal wall it is classified as a sexually transmitted disease. Incubation is typically two to six weeks, but ranges from one week to six months. In immunocompetent patients, individual lesions usually heal spontaneously, without scarring in 2 to 3 months, and the infection clears within 6 to twelve months. In a minority of cases disease persists for up to 5 years. Transmission is through direct skin to skin contact *and* via fomites such as towels or sponges. Lesions that can be mistaken for molluscum include flat warts, condyloma acuminatum, and condyloma lata.

A. Diagnosis

1. History

Most patients present with a complaint of a rash or a "bump" or "warts". Pruritis may be present, as well as inflammation. Atopic dermatitis may be a risk factor.

2. Examination

The lesions are typically smooth spherical papules 2 to 5 mm in diameter with pearly borders and a characteristic central umbilication. The core consists of caseous fluid or a keratotic plug. Larger bumps in groups may occur in people with a weakened immune system (aka giant molluscum). Some patients develop a molluscum dermatitis, characterized by eczematous patches or plaques surrounding the molluscum lesions. Inflammation of molluscum is common and can be a sign of impending regression; it should not be mistaken for secondary infection.

3. Laboratory

There is no specific laboratory test available to diagnose molluscum contagiosum. All patients should have a VDRL (or RPR) done and a full STD evaluation, if indicated.

4. Diagnostic Criteria

- a. Diagnosis is clinical and based on visual inspection of lesions.
- b. Expression of a firm keratotic plug, which may be followed by brisk bleeding, supports the clinical diagnosis.

B. Treatment

1. Molluscum lesions often heal spontaneously. However, treatment may reduce autoinnoculation and transmission to others, may reduce pruritis if present and may help to prevent scarring due to trauma, inflammation or secondary infection.
2. Strong evidence for the efficacy of any particular treatment for molluscum is lacking.

3. Cryotherapy with liquid nitrogen *or* application of podophyllotoxin (in the clinic setting) can be used to treat molluscum in adults, as is done with genital warts. Alternatively patients can be instructed to squeeze the central plug of the lesions to expedite healing. Imiquimod has been shown to be effective in some small studies and offers an option for home treatment, but data is insufficient to consider it a recommended therapy.
4. Cryotherapy to molluscum in dark skinned patients may cause prominent hypopigmentation. Dark-skinned patients should be counseled on risks and benefits of therapy.

C. Follow-up

A single treatment with cryotherapy is generally effective, although the lesion may take several days to weeks to resolve.

D. Counseling/Education

Patients should:

1. Return for evaluation if symptoms recur after treatment.
2. Avoid intimate (direct) contact and sharing of intimate items (towels, sponges) until lesions have disappeared.
3. Be screened for HIV and other STDs according to current clinic protocols.

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. Treatment for HIV infection with highly active antiretroviral therapy (HAART) has been shown to reduce the occurrence of molluscum in HIV-infected patients.

Mucopurulent Cervicitis

Mucopurulent cervicitis (MPC) is a clinical syndrome characterized by a mucopurulent cervical exudate and endocervical friability. Patients may be asymptomatic. *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* are among the pathogens associated with infectious MPC, but in many cases no etiologic organism can be identified. Herpes simplex virus and *Trichomonas vaginalis* can also produce cervicitis but these organisms tend to infect the ectocervix, thereby not creating endocervical mucus. Complications of untreated infection may include the development of endometritis and salpingitis (PID), which may subsequently result in infertility, ectopic pregnancy, or chronic pelvic pain.

Noninfectious cervicitis can result from malignancy, trauma associated with foreign objects (diaphragms, tampons, IUD strings), radiation treatment, sensitivity to irritants (contraceptive jelly, latex, douches, etc.), systemic inflammatory disease (Behcet's syndrome), surgical instrumentation, or idiopathic inflammation of the cervical transformation zone.

A. Diagnosis

1. History

- a. MPC is frequently asymptomatic.
- b. If symptomatic, patient may complain of vaginal discharge, coital or intermenstrual bleeding, pain with intercourse, or pain with urination.
- c. The patient may have a partner who was diagnosed with urethritis.

2. Examination

- a. Mucopurulent cervical discharge. A positive swab test is defined by the finding of exudate (yellow discoloration) on the first swab after insertion into endocervix. It is often helpful to hold the swab against a white paper background for contrast.
- b. Cervical friability (bleeding) is often present after the first swab is inserted. Cervical erythema and edema may also be present.
- c. Cervical motion tenderness may be present and is diagnostic of concurrent [pelvic inflammatory disease](#).

3. Laboratory

- a. A Gram stain of the cervical discharge may reveal white blood cells. The presence of Gram-negative intracellular diplococci suggests gonorrhea as the etiologic agent.
- b. Vaginal wet mount to assess for leukorrhea, trichomoniasis or bacterial vaginosis.
- c. Vaginal swab, cervical swab or urine sample for gonorrhea and chlamydia NAAT testing. Vaginal swabs have the highest sensitivity and are the preferred specimen.
- d. Vaginal swab for trichomoniasis NAAT (if available)

4. Diagnostic Criteria

(requires a or b, and c)

- a. Presence of mucopurulent endocervical exudate or the finding of yellow or greenish exudate on the first white cotton-tipped swab inserted into the endocervical canal (positive swab test). The cytobrush does not count.
- b. Demonstration of cervical bleeding when the first swab is placed in the endocervix (the cytobrush does not count).
- c. Exclusion of other causes of cervicitis.

Note: MPC is a clinical diagnosis; if mucopus is present, a Gram stain should be done to look for white blood cells and for N. gonorrhoeae. If there is microscopic evidence of gonococcal infection, the diagnosis of gonococcal cervicitis should be made.

B. Treatment

The results of the chlamydia and gonorrhea test should determine the need for treatment. Adolescents, patients unlikely to return for treatment, and women at high-risk for chlamydia (e.g., those with prior infection, known recent exposure, new or multiple sex partners, or who are aged ≤ 25) should be treated empirically with a regimen that covers chlamydia:

1. **Azithromycin** 1 g orally once *OR*
2. **Doxycycline** 100 mg orally twice daily for 7 days

Note: Doxycycline is contraindicated during pregnancy and lactation; azithromycin 1 g orally should be used.

Concurrent treatment for [gonorrhea](#) should be administered if gonorrhea is identified on Gram stain, or the patient is in a high-risk group for gonorrhea (age < 25 , previous GC, African-American).

Treatment for [trichomoniasis](#) and/or [bacterial vaginosis](#) should be given if detected on wet mount.

C. Follow-up

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

D. Counseling/Education

Patients should:

1. Be counseled about the potential health consequences of untreated MPC.
2. If prescribed, understand how to take prescribed oral medications.

3. Return for evaluation if symptoms persist or recur after treatment.
4. Based on test results, refer sex partner(s) for examination and treatment or provide them with patient-delivered partner therapy.
5. If treated, abstain from sex for at least 7 days and until sex partners have been treated.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Be screened for HIV and other STDs according to current clinic protocols.

E. Evaluation and Treatment of Sex Partners

Men who are sex partners in the past 60 days of women with MPC should be examined for STDs and treated with the same regimen.

Patient-delivered partner therapy should be given for partners unlikely to come in for evaluation and treatment.

Nongonococcal Urethritis

Symptoms of nongonococcal urethritis (NGU) may include dysuria, a mucoid, mucopurulent, or purulent urethral discharge, and urethral pruritus. The incubation period of NGU is one to five weeks, considerably longer than for gonorrhea (GC). *It is not possible to differentiate GC from NGU based on clinical presentation alone.*

Chlamydia trachomatis (CT) is the most frequent cause of NGU (i.e., 15-40% of cases); however, the prevalence differs by age group, with lower prevalence among older men. Complications of CT-associated NGU include epididymitis, prostatitis and reactive arthritis. *Mycoplasma genitalium* is another cause of NGU. While FDA approved diagnostic tests for *M. genitalium* are not yet widely available, current standard treatments for NGU are effective against chlamydia and moderately effective against *M. genitalium*. Enteric bacteria can cause NGU in men who have insertive anal sex. Other less common causes of NGU include *Trichomonas vaginalis*, primarily in heterosexual men, and HSV. NGU may be acquired through oral-penile contact. HSV, Epstein Barr Virus, and adenovirus have been identified as causative agents. Therefore, it is possible that a patient in a monogamous relationship may develop NGU due to receiving oral sex from his partner. Diagnostic and treatment procedures for the less common causes of NGU are reserved for situations in which NGU is unresponsive to therapy (see [recurrent and persistent urethritis](#)).

In addition to partner referral for evaluation and treatment, patient-delivered partner therapy (PDPT) is important in the clinical management of NGU.

A. Diagnosis

1. History
 - a. Patients usually present with dysuria with or without urethral discharge; if the patient complains of discharge, it is usually mucoid, scant, and may only be present in the morning.
 - b. In general, the symptoms are similar to those of gonococcal urethritis but milder. On occasion the discharge may be mucopurulent or purulent and indistinguishable from gonorrhea on physical examination.
 - 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, “milk” the penis to see if an exudate can be expressed.
3. Laboratory
 - a. If discharge is present, perform a Gram stain to look for white blood cells and Gram-negative diplococci.

- b. If discharge is present, streak the discharge on a modified Thayer-Martin (MTM) plate for GC culture.
- c. Obtain first void urine NAAT for chlamydia and gonorrhea.
- d. If discharge is absent, evaluate the urine for leukocyte esterase (LE).
- e. If LE test is negative, proceed to microscopic examination, if available, of spun urine sediment for WBCs. (Urine centrifuged 6000 rpm x 3 minutes).

4. Diagnostic Criteria

Urethritis can be documented by the presence of any of the following signs:

- a. Mucopurulent or purulent discharge.
- b. Gram stain or methylene blue (MB)/gentian violet (GV) staining of urethral secretions demonstrating ≥ 2 WBCs per high power field (100x). These point of care tests are highly sensitive and specific for documenting both urethritis and the presence or absence of gonococcal infection.
- c. Positive leukocyte esterase test on first-void urine (“small” or greater).
- d. ≥ 10 WBCs per high power field (40x) on spun urine sediment.

5. Further Testing

- a. In patients reporting urethral lesions or significant urethral discomfort without discharge, consider collecting a swab of the meatus for HSV PCR.

B. Treatment

Treatment should be initiated at the time of NGU diagnosis. Empiric treatment of symptomatic men who do not meet objective diagnostic criteria for NGU can be considered if it is thought that the patient is at high risk for infection and is unlikely to return for treatment.

Single-dose regimens offer the advantage of directly observed therapy and should be used if the risk of nonadherence is high. If multiple-dose regimens are used, the full course of medication should be provided in the clinic or health care provider’s office and the first dose should be observed.

Recommended regimens:

1. **Azithromycin** 1 g orally in a single dose *OR*
2. **Doxycycline** 100 mg orally twice daily for 7 days

Alternative regimens:

1. **Ofloxacin** 300 mg orally twice daily for 7 days *OR*
2. **Levofloxacin** 500 mg orally daily for 7 days *OR*
3. **Erythromycin base** 500 mg orally four times daily for 7 days

C. Follow-up

Patients should be instructed to return for evaluation if symptoms persist or recur after completion of therapy. Symptoms alone without documentation of urethral inflammation are not a sufficient basis for re-treatment. Refer to section on [recurrent and persistent urethritis](#) for additional details.

All patients who are diagnosed with GC or CT urethritis should return in 3 months for repeat testing for these organisms, since these individuals are at high-risk for repeat infection.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refer sex partner(s) from the past 60 days for evaluation and testing, and offer patient-delivered partner therapy (PDPT) for these partners
4. Avoid sex for at least 7 days and until partner(s) are treated.
5. Understand that oral flora may cause urethritis, and thus NGU can develop after oral sex with a monogamous partner.
6. Be offered condoms and advised that condoms can prevent future infections.
7. Be screened for HIV and other STDs according to current clinic protocols.
8. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

All sex partners within the prior 60 days of patients who have NGU infection should be examined, tested, and empirically treated with an appropriate regimen. Patient delivered therapy with **azithromycin** 1 g orally once or **doxycycline** 100 mg orally twice a day for 7 days may be treatment options for patients or partners unlikely to come in for examination.

Patients should be instructed to refrain from having sex for one week after treatment is initiated, and should not resume sexual activity with their partner until one week after the partner initiates treatment. Some patients think that it is safe to have unprotected sex if both they and their partner(s) are taking medication simultaneously. Even if a one-time dose of medication is prescribed patients should be instructed to avoid sex for 7 full days.

Recurrent and Persistent Urethritis

Recurrent NGU is a common problem. Objective signs of urethritis should be confirmed by the clinician before consideration of additional antimicrobial therapy. Optimal regimens for treating patients who have persistent symptoms or frequent recurrences after treatment of NGU have not been identified. Patients can be re-treated with the initial regimen if they did not adhere to the treatment or are likely to have been re-exposed to an untreated sex partner. When reinfection is unlikely, the most common cause of persistent or recurrent NGU is *M. genitalium*. *Trichomonas* may cause urethritis in men who have sex with women. Oral sex can be associated with NGU; HSV, adenovirus and normal oral flora may be causative organisms and can contribute to recurrent or persistent urethritis. Persistent perineal, penile or pelvic pain, pain with urination, or pain during or after ejaculation may be secondary to chronic prostatitis or chronic pelvic pain syndrome and should prompt referral to a urologist if symptoms persist despite evaluation and management as outlined below.

A. Diagnosis

1. Verify diagnosis of urethritis by microscopic evaluation of urethral discharge, leukocyte esterase urine test, or examination of urine sediment (see [NGU: diagnostic criteria](#)).
2. In patients reporting significant dysuria with scant discharge, obtain a HSV PCR of urethral meatus.
3. For men who have sex with women, consider sending a urine trichomoniasis NAAT test if available.

B. Treatment

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

1. If treated with **Doxycycline** originally, treat with **Azithromycin** 1 g orally once
2. If treated with **Azithromycin** originally, treat with **Moxifloxacin** 400 mg orally daily x 7 days
3. In areas with high prevalence of Trichomoniasis (and if trichomoniasis NAAT testing is unavailable), add the following medication for men who have sex with women (to either **Azithromycin** or **Moxifloxacin** as outlined above):
 - a. **Metronidazole** 2 g orally once *OR*
 - b. **Tinidazole** 2 g orally once

If trichomoniasis NAAT testing is available, treatment for trichomoniasis should be based on the results of the NAAT test.

4. If the patient reports any of the following symptoms, consider a trial of treatment for [HSV](#): Prominent dysuria or urethral discomfort with scant discharge; Meatal erythema or ulceration; Tender penile edema; Inguinal lymphadenopathy; Constitutional symptoms

C. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refer sex partner(s) for evaluation and treatment.
4. Avoid sex for at least 7 days and until partner(s) are treated.
5. Be offered condoms and advised that condoms can prevent future infections.
6. Be screened for HIV and other STDs according to current clinic protocols.

Specific messages to stress:

1. Urethritis is likely to be a sexually transmitted disease.
2. Laboratory tests are not 100% accurate.
3. Laboratory tests to identify all pathogens that can cause urethritis are not available.
4. Adenoviruses and oral flora obtained by receiving oral sex may also be associated with NGU and there is no specific therapy for these organisms.
5. It is important for female partners to be examined as pathogens may be more easily identified in the partner (e.g., trichomonas).

D. Evaluation of Sex Partners

Sex partners of patients with recurrent NGU should be evaluated and tested. Consider obtaining a wet mount to evaluate for trichomoniasis in female partners of male patients with recurrent NGU.

Patients should be instructed to refrain from having sex for one week after treatment is initiated, and should not resume sexual activity with their partner until one week after the partner initiates treatment. Some patients think that it is safe to have unprotected sex if both they and their partner(s) are taking medication simultaneously. Even if a one-time dose of medication is prescribed patients should be instructed to avoid sex for 7 full days.

Pelvic Inflammatory Disease

Pelvic inflammatory disease 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. The resulting infection may include endometritis, salpingitis, oophoritis, tubo-ovarian abscess, perihepatitis and pelvic peritonitis. Much is still unknown regarding the microbiology of PID. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are implicated in less than half of cases, but many other organisms including *Haemophilus influenzae*, *Gardenerella vaginalis*, enteric Gram-negative rods, *Streptococcus agalactiae*, *M. genitalium*, *M. hominis*, and *U. urealyticum* have been associated with PID as well. Regardless of laboratory findings, PID should always be treated as a mixed, polymicrobial infection.

Many women with PID have no symptoms, nonspecific symptoms (dyspareunia, abnormal vaginal bleeding, vaginal discharge) or just mild-to-moderate lower abdominal pain and tenderness; indeed, many women with late complications of PID (e.g., infertility or ectopic pregnancy) report no known history of PID. Occasionally, acute infection becomes life threatening because of extensive peritonitis, which is usually caused by a rupture of a tubo-ovarian abscess. Other complications and medical consequences include chronic pelvic pain, and pelvic adhesions requiring subsequent surgery.

Absolute diagnostic criteria for PID remain uncertain. The "gold standard" has been laparoscopic evidence of tubal inflammation. Routine use of laparoscopy to diagnose PID is impractical. Therefore, less reliable clinical criteria must be used. In the past PID has been described as "mild" or "severe". These are very poor descriptors since PID reflects the site(s) of infection, not the degree of symptomatology. As stated above, women with very mild symptoms may have extensive disease and resultant infertility. A patient who meets the criteria for PID may be treated as an outpatient if she appears to be clinically stable, is reliable and does not fall into one or more of the categories listed below.

A. Diagnosis

Although the clinical diagnosis of PID is imprecise, given the risk of significant reproductive sequelae, providers should maintain a low clinical threshold for diagnosis. PID should always be considered in women with cervical, uterine or adnexal tenderness.

1. History

Patients may complain of focal or diffuse lower abdominal pain, fever, vaginal discharge, or pain with intercourse. Menstrual abnormalities are common. Nausea and vomiting may be present but are nonspecific. 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 vaginal or cervical discharge, and cervical, uterine or adnexal tenderness.
- c. Abdominal exam to assess for peritoneal signs (rebound, guarding) or focal tenderness.

3. Laboratory

- a. Perform pregnancy test in all patients with suspected PID.
- b. Wet prep of vaginal secretions to assess for [bacterial vaginosis](#):
 1. Evaluate KOH whiff test
 2. Evaluate for clue cells
 3. Quantify WBC/HPF
 4. Check vaginal pH.
- c. Gram stain of cervical discharge to look for white blood cells and gonococci.
- d. Vaginal or cervical swab for GC and CT NAAT.
- e. Vaginal swab for trichomoniasis NAAT (if available)
- f. Test for syphilis and HIV
- g. Urine dipstick and urine microscopy if patient reports dysuria, frequency or urgency, or has suprapubic tenderness on exam

4. Diagnostic Criteria

Empiric treatment of PID should be initiated in sexually active young women and other women at risk for STDs if the following minimum criteria are present:

- a. Lower abdominal or pelvic pain **and**
- b. Cervical motion tenderness **or** uterine tenderness **or** adnexal tenderness **and**
- c. Absence of other causes of pelvic pain (e.g., ectopic pregnancy, appendicitis)

Additional criteria useful in diagnosing PID:

- a. Oral temperature > 38.3°C (101°F)
- b. Abnormal cervical or vaginal discharge
- c. Cervical friability
- d. Presence of white blood cells (> 10 WBC/HPF) on saline microscopy of vaginal secretions.
- e. Evidence of cervical infection with *N. gonorrhoeae* or *C. trachomatis*.

Other diagnostic criteria (not available at City Clinic):

- a. Elevated erythrocyte sedimentation rate (ESR) or c-reactive protein (CRP).
- b. Histopathologic evidence of PID on endometrial biopsy.
- c. Characteristic findings with transvaginal sonography, CT, MRI, or during laparoscopy.

B. Treatment

1. Outpatient treatment is standard in those patients with mild to moderate symptoms, able to tolerate the medications, and willing to return for frequent assessments.

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

- a. Regimen A

Ceftriaxone 250 mg IM once *AND*

Doxycycline 100 mg orally twice daily for 14 days

PLUS, if patient is diagnosed with bacterial vaginosis:

Metronidazole 500 mg orally twice daily for 14 days

- b. Regimen B (not available at City Clinic)

Cefoxitin 2 g IM once *AND*

Probenecid 1 g orally once *AND*

Doxycycline 100 mg orally twice daily for 14 days

PLUS, if patient is diagnosed with bacterial vaginosis:

Metronidazole 500 mg orally twice daily for 14 days

- c. Regimen C (not available at City Clinic)

Other **parenteral third-generation cephalosporin** (e.g., ceftizoxime or cefotaxime) *AND* **Doxycycline** PLUS **Metronidazole** if BV is present.

- d. Alternative Oral Regimens

Information regarding other outpatient regimens is limited, but one other regimen has undergone at least one clinical trial and has broad-spectrum coverage. Amoxicillin/clavulanic acid plus doxycycline was effective in obtaining short-term clinical response in a single clinical trial. Gastrointestinal symptoms might limit the overall success of this regimen.

Several recent investigations have evaluated the use of azithromycin in the treatment of upper-reproductive tract infections; however, the data are limited. Ceftriaxone plus azithromycin instead of doxycycline is an option in potentially

nonadherent patients; the suggested dose is azithromycin 1 g orally x 1 followed by a second 1 g dose one week later.

There are no studies evaluating the efficacy of oral cephalosporins in the treatment of PID.

e. Alternative Oral Regimens with Quinolones

Given the prevalence of quinolone-resistant GC, the use of quinolones is no longer recommended for PID treatment. However, if parenteral cephalosporin treatment is not possible the following can be used if the risk of GC is low:

Levofloxacin 500 mg once daily for 14 days *OR* **Ofloxacin** 400 mg twice daily for 14 days *OR* **Moxifloxacin** 400 mg once daily for 14 days (with or without Metronidazole)

If a quinolone regimen is used diagnostic testing for GC is critical and, if GC is diagnosed, treatment should be based on antimicrobial susceptibility, when possible. If quinolone-resistance is found or if susceptibility testing is not possible, parenteral cephalosporin treatment is recommended.

2. Hospitalization is recommended in the following situations:*

- a. Surgical emergencies such as appendicitis or ectopic pregnancy cannot be excluded.
- b. A pelvic abscess is suspected.
- c. The patient is pregnant.
- d. Patient compliance is uncertain.
- e. Severe illness precludes outpatient management (e.g., temp > 38.3°C, 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 SFGH ER, treatment should be instituted (as per guidelines above) before patient leaves SF City Clinic as failure to follow-up at SFGH ER is often a problem.*

C. Follow-up

Patients should be rechecked three days after diagnosis (or within 2-4 days depending on which day of the week she was diagnosed).

Follow-up at three days should establish:

1. Patient adherence to medications.
2. Symptomatic improvement.
3. Clinical improvement as documented by a repeat bimanual examination.

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

D. Counseling/Education

Patients should:

1. Be counseled about the risks of PID and routes of transmission.
2. Be advised to seek care at an ER if there is sudden worsening of symptoms and SFCC is not open.
3. Understand how to take prescribed oral medications.
4. Return three days after initiation of therapy for repeat evaluation.
5. Be counseled to notify sex partners from the past 30 days and refer them for evaluation and treatment, or provide them with patient-delivered partner therapy.
6. Avoid sex until patient and partner(s) have completed treatment (at least 14 days).
7. Receive contraceptive counseling, if an IUD was removed (see below).
8. Be advised to return in 3 months for repeat testing to rule out re-infection.
9. Be offered condoms and advised that condoms can prevent future infections.
10. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

All sex partners in the prior 60 days of patients who have been diagnosed with PID should be examined, tested, and empirically treated for *N. gonorrhoeae* and *C. trachomatis*.

Patient-delivered partner therapy (PDPT) with cefixime 400 mg orally once and azithromycin 1 g orally once can be offered to patients with PID, particularly if they report that it is unlikely that their partners will present to a clinic for evaluation. If a diagnosis of GC is confirmed, patients should inform their partners that it is optimal for them to come to a clinic to receive an injection of ceftriaxone (in addition to oral azithromycin), and be screened for other STDs.

F. Special Considerations

Intrauterine device: The risk for IUD-associated PID is limited to the first three weeks after insertion and evidence is insufficient to routinely recommend IUD removal in women diagnosed with PID. In compliant patients with uncomplicated PID, the IUD may be left in place during antimicrobial treatment if the woman desires to continue with the IUD as a contraceptive method. Reinforce with the patient that this approach requires close follow-up with a repeat exam in 2 to 3 days. If there is no clinical improvement at the time of follow-up, IUD removal may be considered. If the IUD is removed, contraceptive counseling is necessary.

Proctitis

Sexually transmitted gastrointestinal syndromes include proctitis, proctocolitis, and enteritis. While rectal gonococcal, chlamydial, and herpetic infections are acquired through receptive anal intercourse, sexually transmitted enteric infections occur primarily as a result of sexual practices that involve fecal-oral transmission (anilingus). For all these syndromes, the majority of patients are men who have sex with men and trans women who have sex with men. This protocol will only present the diagnostic workup and treatments for proctitis. Patients who present with enteric symptoms (e.g., diarrhea or abdominal cramps) should be referred to the Zuckerberg San Francisco General Emergency Room or urgent care, Tom Waddell Clinic, district health centers, or their private providers where they can receive an evaluation that includes a stool analysis for ova, parasites, and bacteria.

Proctitis is inflammation limited to the rectum and is associated with anorectal pain, tenesmus, and discharge. *Neisseria gonorrhoeae*, *Chlamydia trachomatis* (including LGV serovars L1-L3), Herpes simplex virus types I and II and syphilis are the most common sexually transmitted pathogens involved. Inflammatory STDs such as CT or GC and ulcerative STDs such as HSV greatly increase the risk of HIV transmission. If infectious proctitis is diagnosed in an HIV-negative patient, they should receive enhanced risk reductive counseling from a health worker or disease control investigator (DCI).

A. Diagnosis

1. History
 - a. Patients present with symptoms referable to the rectum: rectal pain, tenesmus, and discharge.
 - b. Patients will typically have a remote or recent history of receptive anal intercourse.
2. Examination
 - a. With the patient on a proctology table, first examine the external perianal area and visible anal canal looking for lesions, ulcers, or rash.
 - b. Using the anoscope examine the rectal mucosa. Sample either the mucosal wall or any discharge with a swab to obtain material for Gram stain, GC/CT NAAT and both HSV and LGV PCRs. Note any friability or frank bleeding.
3. Laboratory
 - a. Gram stain rectal discharge from anoscopy.
 - b. Obtain a rectal swab for chlamyda and gonococcal NAAT.
 - c. Obtain a rectal swab in viral transport media for reflex LGV testing, performed by the SFDPH Public Health Lab if the rectal Chlamydia NAAT is positive (see [LGV](#))
 - d. Obtain a HSV PCR even if no obvious lesions are present.

- e. Serum VDRL (or RPR).
- f. Rapid HIV antibody test (if not known to be HIV-positive).

4. Diagnostic Criteria

Anorectal exudate detected on examination or WBCs on Gram stain of rectal discharge provide presumptive evidence of proctitis.

B. Treatment

Treatment should cover *N. gonorrhoea* and *C. trachomatis*. Consider additional empiric treatment for HSV or LGV if clinical suspicion is high.

Recommended regimen:

Ceftriaxone 250 mg IM in a single dose once and **doxycycline** 100 mg orally twice daily for 7 days

If gram stain of rectal discharge is positive for intracellular gram negative diplococci:

Consider using **Azithromycin** 1 g orally once, instead of **doxycycline**, in combination with **Ceftriaxone** for treatment of GC proctitis.

If there is a high suspicion for [HSV infection](#) (painful perianal or rectal mucosal ulcers):

Consider adding **Acyclovir** 400 mg orally three times daily for 7-10 days for HSV infection

If there is a high suspicion for [LGV infection](#) (bloody discharge, perianal or mucosal ulcers) use the following regimen:*

Ceftriaxone 250 mg IM in a single dose once and **doxycycline** 100 mg orally twice daily x 21 days

**The attending physician should be notified of possible LGV cases.*

C. Follow-up

Patients diagnosed with GC or CT should return for repeat testing (by rectal NAATs) in 3 months due to high rates of repeat infection in these individuals.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed medication.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refer sex partners from the past 60 days for evaluation.
4. Avoid sex (including both anilingus and anal receptive sex) for at least 7 days and until partner(s) are evaluated and treated.
5. Be advised to return in 3 months for repeat testing to rule out re-infection.
6. Be screened for other STDs according to current clinic guidelines.

7. Be counseled about PrEP if at elevated risk for HIV-infection. In addition, PrEP should be recommended to all MSM and trans patients with confirmed proctitis.

E. Evaluation and Treatment of Sex Partners

Sex partners in the past 60 days of patients with proctitis should be given patient-delivered partner therapy for gonorrhea and chlamydia and referred for further evaluation.

Pubic Lice (Crabs)

Crab lice, *Phthirus pubis*, usually infest the hairy parts of the pubic area but may also infest facial hair and eyelashes. 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 (e.g., staphylococcus or streptococcus) 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. Light microscopy will identify lice or nits.
 - b. If any type of unusual rash is present in the genital area, the patient should have a stat RPR as well as VDRL (or RPR) to assess for syphilis.
 - c. Additional STD testing as indicated by exposure history and clinic screening guidelines.
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

Recommended regimens:

1. **Permethrin** (1%) creme (Nix) rinse applied to the affected area and rinsed off in 10 minutes. This is the treatment of choice as permethrin is the most studied and least toxic to humans. Has residual activity even after rinsing.

2. **Pyrethrins** and **piperonyl butoxide** (RID, Triple X, A-200) applied to the affected area and washed off in 10 minutes. No residual activity after rinsing, so repeat application in 1 week.

Resistance to permethrin and pyrethrins and piperonyl butoxide has been increasing and is widespread, but because of long duration of application and side effects associated with alternative regimens, these are still the recommended first line regimens for pubic lice.

Alternative regimens (use when treatment failure is suspected to occur as a result of resistance):

1. **Malathion** 0.5% lotion applied for 8-12 hours and washed off
2. **Ivermectin** 250 mcg/kg orally, repeated in 2 weeks (contraindicated in pregnancy)

*Do not use any of the above for infestation of the eyelashes; see [section F](#): special considerations for recommended treatment.

Although data supporting its efficacy are limited, we recommend combing the affected area with a fine-toothed comb after treatment– this may help remove eggs that would otherwise hatch and prolong infestation.

C. Follow-up

Louse egg incubation is 6-8 days. Thus patients should therefore be re-evaluated 7-10 days after treatment if symptoms persist. If lice are found or nits are observed at the hair-skin junction, retreat with an alternative regimen.

D. Counseling/Education

Patients should:

1. Understand how to apply prescribed medication.
2. Return 7-10 days after treatment for evaluation if symptoms persist.
3. Refer sex partner(s) for evaluation and treatment (particularly if PDPT is not provided).
4. Avoid sex for at least 7 days and until partner(s) are treated and bedding and clothing have been decontaminated.
5. Be screened for HIV and other STDs according to current clinic protocols.

E. Evaluation and Treatment of Sex Partners

Sex partners within the previous month should be treated. Patient-delivered partner therapy (PDPT) can be offered for current or recent partners. Asymptomatic non-sexual household contacts do not need to be treated as contacts.

F. Special Considerations

1. 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.
2. Pediculosis of the eyelashes should be treated by the application of occlusive ophthalmic ointment (by prescription) or Vaseline (may be more irritating than the prescription ointment) to the eyelid margins, twice daily for ten days to smother lice and nits.

Scabies

The itch mite, *Sarcoptes scabiei*, can penetrate 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 are likely on the penis and scrotum. 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 for 1-2 weeks even after mites are dead. Individuals with a prior history of scabies may have more rapid onset of symptoms due to prior sensitization. Complications include secondary infections due to scratching.

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. Look for nodules on the male genitals. 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 scalpel with oil on it so skin scrapings stay on scalpel. 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.
- b. Patients who have genital lesions should have a stat RPR done to rule out syphilis before establishing a diagnosis of scabies.

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 on typical sites.

- c. Sexual exposure or close physical contact to a person infested with scabies mites.
- d. Exclusion of syphilis, if necessary.

B. Treatment

Recommended:

1. **Permethrin** cream 5% applied from the neck down and washed off after 8-14 hours. Medication comes in a 60 g tube half to be applied for the first treatment, and 2nd half to be applied 1 week later. Permethrin is not contraindicated in pregnancy or during lactation. Patients should be informed that pruritus may persist for 1-2 weeks after therapy.

OR

2. **Ivermectin** 200 ug/kg orally with food once, repeated in 2 weeks (food increases bioavailability of drug and skin permeation).

Alternative:

1. **Lindane** (1%) 1 oz of lotion or 30 g of cream applied in a thin layer to all areas of the body from the neck down and thoroughly washed off after 8 hours. Lindane should NOT be applied immediately after a bath or shower, in patients with extensive dermatitis or in children < 10 years old. Lindane is contraindicated in pregnant or lactating women.

C. Counseling/Education

Patients should:

1. Understand how to apply prescribed medication.
2. Return after two weeks for evaluation if symptoms persist (patients should be informed that pruritus is a hypersensitivity reaction and so may persist for several weeks even after successful treatment).
3. Refer sex partner(s) for treatment.
4. Avoid sexual or intimate contact until patient and partner(s) are fully treated.
5. Be screened for HIV and other STDs according to current clinic protocols.

D. Evaluation and Treatment of Sex Partners

Persons who have had sexual, close personal, or household contact with the patient within the month preceding scabies infestation should be examined or empirically treated (i.e. offered patient delivered partner therapy).

E. Special Considerations

Decontamination of articles: Clothing, bed linens, and towels that may have been contaminated 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.

Persons with HIV infection with uncomplicated scabies should be treated in the same manner as HIV negative individuals. Persons with HIV and other immunocompromised states are at risk for crusted scabies. Speciality consultation should be sought if crusted scabies is suspected.

Syphilis

Syphilis is caused by the spirochete, *Treponema pallidum*. Syphilis has been divided into four stages (primary, secondary, latent, and tertiary), which reflect the clinical progression of disease.

Primary syphilis is typically characterized by a painless, indurated ulcer (chancre) that appears at the site of infection by *T. pallidum* about 21 days (the range is 10-90 days) after exposure and lasts from one to five weeks. The regional lymph nodes may become mildly to moderately enlarged but are not tender.

Secondary syphilis, which usually appears days to weeks after the primary chancre has healed, is characterized by a skin rash, mucous patches, and *condyloma lata* sometimes accompanied by generalized lymphadenopathy, headache, sore throat and fever. These manifestations disappear spontaneously within two to six weeks but may recur within the first year after infection.

Latent syphilis is characterized by the absence of symptoms or signs in the presence of reactive nontreponemal and treponemal serologic tests. The onset of latent syphilis is considered to occur when secondary recurrences become much less likely, and has arbitrarily been divided into early latent syphilis (duration of less than one year) and late latent syphilis (duration of more than one year).

Tertiary syphilis includes cardiovascular syphilis (thoracic aortic aneurysm, aortic valve disease), neurologic disease (general paresis, tabes dorsalis), and gumma formation.

Neurosyphilis may occur at any stage of the disease. There is no commercially available test for neurosyphilis that is both sensitive and specific. A reactive VDRL of the cerebrospinal fluid is confirmatory but studies show a variable sensitivity for this test of 30-70%. Lumbar puncture should be done if there are symptoms or signs suggestive of CNS involvement no matter what the stage of infection.

Syphilis in Special Populations

HIV-Infected Persons:

Unusual serologic responses have been observed among HIV-infected individuals who are co-infected with syphilis. Most reports have involved titers that were higher than expected, but false negative results or delayed responses have also been reported. Nevertheless, both treponemal and nontreponemal serologic tests for syphilis are accurate for the majority of patients with syphilis and HIV co-infection.

Pregnancy:

Due to the devastating impact of syphilis on the fetus, special precautions must be taken with women of childbearing age with syphilis. **All women diagnosed with any stage of syphilis must have a stat urine pregnancy test.** If the test is positive, she must be counseled concerning syphilis, pregnancy and risk to the fetus. She should be treated with penicillin as indicated by stage of infection and a prenatal care appointment should be made for her. Pregnant women

with syphilis are a high priority for the department of public health. The health department must be contacted within 24 hours of any suspected or confirmed syphilis case and can assist providers in ensuring that pregnant women with syphilis are adequately treated.

A. Stages of Syphilis

Primary Syphilis

1. History

- a. Patients may present with a genital, anal, or oral ulcer. Known as a chancre this lesion is classically painless, with rolled, indurated borders, although atypical lesions are possible. The chancre appears 10-90 days (average 21 days) after contact with an infected partner, so the date of the last sexual exposure should be documented. Multiple chancres are more likely to be seen in HIV-positive individuals.
- b. Patients should be questioned regarding neurologic symptoms (see [neurosyphilis](#)).
- c. Refer to the [genital ulcer protocol](#) for other features to elicit from the history.

2. Examination

- a. All possible exposed sites should be carefully examined.
- b. Refer to the [genital ulcer protocol](#) for the characteristics of the ulcer(s) and lymph nodes that should be evaluated and noted.
- c. Chancres may be atypical: for example they may lack induration, have flat rather than rolled edges, and be painful. Atypical chancres are more likely in patients who have had previous cases of syphilis.
- d. A neurological exam should be performed (see [neurosyphilis](#)).

3. Laboratory

- a. A darkfield microscopic exam of the ulcer should be done. Darkfield microscopy is a highly sensitive method by which to diagnose primary syphilis (up to 95% sensitive in experienced hands). Do not perform darkfield on oral cavity lesions because exams at this site are difficult to interpret due to the presence of non-pathogenic spirochetes. Lesions on the lips may be successfully evaluated with the darkfield exam.

To identify spirochetes by darkfield microscopy:

1. The lesion should be cleaned and gently abraded with a gauze pad moistened with saline and gently squeezed until a small amount of serous fluid is expelled.
2. The serous fluid should be placed on the underside of a cover slip and then firmly pressed onto a glass slide for darkfield microscopy.
3. The specimen should be examined immediately.

4. A minimum of 25 or more fields should be examined before determining that spirochetes are not present; performing second and third darkfield exams on all lesions is indicated if there is a strong suspicion of syphilis.
 5. All positive, and whenever possible, all negative, darkfield exams should be reviewed by the attending physician.
 6. *T. pallidum* has 6 to 14 regular spirals, rotates smoothly, may move forward and backward through the field, and usually gently bends at right angles along the longitudinal axis.
 7. Many patients with genital lesions apply topical treatments to their lesions, which may produce a negative darkfield exam.
- b. All ulcerative lesions should be swabbed for HSV PCR. At present the Public Health Lab does not perform culture for *H. ducreyi* (the agent of chancroid).
 - c. All patients must have a stat RPR, except for those with a positive darkfield exam.
 - d. Both a nontreponemal test (RPR or VDRL) **and** treponemal test (TPPA) should be performed. Nontreponemal tests may be nonreactive in the primary stage (70-75% sensitivity) for up to 10 days after the appearance of the chancre. Because the TPPA may turn positive before the non-treponemal antibody test in primary syphilis, the TPPA should be specifically ordered in patients with a lesion suspicious for primary syphilis such that the lab will run the test even if the VDRL is negative.
 - e. Stat TPPA (Syphilis Health Check™) may provide additional diagnostic information in patients with a genital ulcer when the darkfield is negative and the stat RPR is negative or weakly reactive. This test should only be used in patients who do not have a prior history of syphilis.
 - f. Because syphilis is associated with an increased risk of HIV infection, HIV counseling and testing should be strongly encouraged.
 - g. Patients who have neurologic symptoms or signs should have a lumbar puncture (see [neurosyphilis](#)).

4. Diagnostic Criteria

- a. Identification of *T. pallidum* from an ulcer (i.e., chancre) by darkfield microscopy.
- b. Clinical findings consistent with primary syphilis (i.e., chancre) in a patient with a positive treponemal antibody test (nontreponemal tests may be negative in primary syphilis).
- c. Individuals with reactive nontreponemal tests and nonreactive treponemal tests are considered to be biologic false-positives (BFP). They do not have syphilis and do not require treatment.

Secondary Syphilis

1. History

- a. Patients may present with a rash (may be on the genitals, the palms and soles, or generalized), patchy hair loss (moth-eaten appearance), or white, grey or flesh-colored lesions in the oral cavity (mucous patches) or in the anogenital region (*condyloma lata*). The rash is rarely pruritic and is never vesicular.
- b. Constitutional symptoms may be present, especially in HIV-positive persons. Assess the patient for fever, headache, fatigue, sore throat, or night sweats.
- c. Ask the patient about recent sores in genital, oral, and anal regions, and swollen lymph nodes.
- d. Patients should be questioned regarding neurologic symptoms (see [neurosyphilis](#)).

2. Examination

- a. A complete exam including the oral cavity (mucous patches, chancre), anogenital region (*condyloma lata*, chancres, mucous patches, rash), skin (including chest, back, palms and soles), and lymph nodes (including neck, axilla, epitrochlear and inguinal) should be done. Any rash on the genitals, especially on the scrotum should be suspect for syphilis.
- b. The rash of secondary syphilis is bilaterally symmetrical, and can often be varied, presenting as maculopapular, moist papules or pustules, or as dry and psoriasiform lesions. The only manifestation not consistent with secondary syphilis is a vesicular rash (except in congenital syphilis which may include a bulbo-vesicular rash).
- c. A neurological exam should be performed (see [neurosyphilis](#)). The neurological examination should include an assessment of the following:
 1. Pupils (equal, round, reactive to light?)
 2. Extraocular movements
 3. Smile, lid closing, forehead raise
 4. Hearing
 5. Gait

3. Laboratory

- a. Moist lesions of secondary syphilis (e.g., *condyloma lata*) should be examined by darkfield microscopy. Do not attempt to perform a darkfield exam on dry lesions.
- b. All patients must have a stat RPR (100% sensitive in secondary syphilis), unless there is a positive darkfield from a *condyloma lata*. There have been case reports of patients who have secondary lesions, but negative serologies. Such rare cases should undergo biopsy of a typical lesion to evaluate for *T. pallidum*.
- c. Patients who have neurologic symptoms or signs should have a lumbar puncture (see [neurosyphilis](#)).

4. Diagnostic Criteria

- a. Identification of *T. pallidum* from material from cutaneous or mucous membrane lesions by darkfield microscopy.
- b. Reactive nontreponemal (VDRL or RPR) and treponemal tests and no history of syphilis or a fourfold or greater increase in titer on a nontreponemal test compared with the most recent test for persons with a history of syphilis (compare the same test method, i.e. VDRL for both, or RPR for both) and any one of the following skin or mucous membrane lesions of secondary syphilis:
 1. Skin lesions (bilaterally symmetrical, macular, papular, follicular, papulosquamous, or pustular). There may also be lesions on the face known as nickel and dime lesions (annular syphilids) or split papules in the nasolabial folds, commissures of the mouth or under the ear lobes.
 2. *Condyloma lata* (moist papules, usually in anogenital region or other moist skin areas).
 3. Mucous patches of the oropharynx, labia, vagina, cervix or the glans or prepuce of uncircumcised men.
 4. Alopecia of head hair or loss of the eyelashes and lateral third of the eyebrows.

Early Latent Syphilis

No signs of syphilis on exam, and date of infection thought to be within the past year.

1. History

- a. Patient may have a history of contact to syphilis or may be able to recall recent ulcer or rash.
- b. More often, however, patient cannot recall contact or symptoms.

2. Examination

- a. Patient must have complete physical exam to assess for signs of primary or secondary syphilis.
- b. A neurological exam should be performed (see [neurosyphilis](#)).

3. Laboratory
 - a. VDRL (or RPR)
4. Diagnostic Criteria
 - a. Positive nontreponemal and treponemal test and one of the following:
 1. Documented seroconversion or a sustained (>2 week) fourfold or greater increase in nontreponemal test titers (e.g. 1:4 -> 1:16); OR
 2. Unequivocal symptoms of primary or secondary syphilis in past year OR
 3. A sex partner documented to have primary, secondary, or early latent syphilis OR
 4. Only possible exposure to syphilis was in the last year

Late Latent Syphilis

No signs of syphilis on exam, and date of infection thought to be a year or more prior.

1. History
 - a. Patient may have history of contact to syphilis or may be able to recall ulcer or rash.
 - b. More often, however, patient cannot recall contact or symptoms.
 - c. Patient may have a history of inadequately treated syphilis in the past or incomplete documentation of treatment.
 - d. Patient should be questioned regarding the presence of neurologic symptoms (see [neurosyphilis](#)).
2. Examination
 - a. Patient must have complete exam to carefully evaluate for signs of primary and secondary syphilis.
 - b. A neurological exam should be performed (see [neurosyphilis](#)).
3. Laboratory
 - a. The only laboratory evidence of latent syphilis is a reactive VDRL (or RPR) with a positive TPPA. On occasion the nontreponemal test may be nonreactive.
 - b. A lumbar puncture be done in late latent syphilis if a patient has any of the following (see [neurosyphilis](#)):
 1. Neurologic or ophthalmologic symptoms or signs
 2. Evidence of active disease, such as aortitis, gumma, or iritis
 3. Treatment failure

4. Diagnostic Criteria

- a. A reactive treponemal test in a patient with no prior history of syphilis, absence of symptoms and signs of syphilis, *and* no documentation of a nonreactive syphilis test in the past year.
- b. A fourfold or greater rise in titer of a nontreponemal (VDRL, RPR) test in a patient with a history of syphilis whose last known nontreponemal test was more than one year before. This may represent early latent disease; consult with attending physician on case-by-case basis.

Neurosyphilis

Neurosyphilis can occur at any stage of disease, but in the modern era, most neurosyphilis occurs during early syphilis.

1. History

- a. Patients with acute syphilitic meningitis, which usually occurs in patients with early syphilis, may complain of headache, fever, photophobia, neck stiffness, nausea, vomiting, papilledema, blurred vision, seizures, dizziness, aphasia, focal weakness, trouble speaking, hemiplegia, or cranial nerve palsies (including hearing loss). Any neurologic symptom may be consistent with neurosyphilis.
- b. Ocular syphilis typically presents with blurry vision and other visual changes. Uveitis is the most common finding on ophthalmologic exam, but any eye structure can be involved. Ocular syphilis should be treated as neurosyphilis, even if the LP results are normal.
- c. Patients with general paresis or tabes dorsalis, which are neurologic complications of late syphilis, may present with dementia, psychosis, gait disturbances, lightning pains, or incontinence.

2. Examination

- a. Neurologic examination should include an assessment of the following:
 1. Pupils (equal, round, reactive to light?)
 2. Extraocular movements
 3. Smile, lid closing, forehead raise
 4. Hearing
 5. Gait
- b. If there are symptoms or signs suggestive of neurosyphilis, the patient should be referred to ZSFG Emergency Department for CSF analysis, evaluation and treatment. If the patient has insurance and a primary care provider the patient can follow-up there for the neurosyphilis evaluation. It is appropriate to call that provider with the patient's permission to facilitate this follow-up. The attending physician should be notified of possible neurosyphilis cases.

In general, benzathine penicillin therapy is often initiated prior to LP, but LP should be done as soon as possible.

3. Laboratory

- a. Obtain nontreponemal (VDRL or RPR) and treponemal (TPPA) tests.
- b. A lumbar puncture should be performed. CSF should be sent for cell count with differential, glucose, total protein and CSF VDRL.

4. Diagnostic Criteria

- a. Identification of *T. pallidum* in CSF or CNS tissue by PCR, animal inoculation, DFA, or histology (not done in routine clinical practice).
- b. Clinical suspicion of neurosyphilis **and**
 1. Positive CSF VDRL (this is considered “confirmed”) **OR**
 2. Abnormal CSF WBC > 5 cells/ μ l* or CSF protein > 40 mg/dl (this is considered “probable”)

**Note: In HIV-positive patients, there may be a mild elevation of CSF WBC due to HIV itself, so a more appropriate diagnostic criterion for neurosyphilis in patients with HIV is > 20 WBC/ μ l in patients. Cases of suspected neurosyphilis should be discussed with the attending physician.*

B. Treatment

Obtain a non-treponemal antibody test (VDRL or RPR) on the day treatment for syphilis is initiated.

1. Early Syphilis (less than 1 year duration)
 - a. **Benzathine penicillin G** 2.4 million units IM once.
 - b. For non-pregnant patients who are penicillin-allergic or refuse penicillin therapy, **doxycycline** 100 mg orally twice daily for 14 days may be substituted. This includes HIV-positive individuals.*

Pregnant women with early syphilis must be treated with 2.4 million units of **benzathine penicillin G** (desensitization is necessary if the patient is allergic to penicillin).
2. Late Syphilis (greater than 1 year duration or of unknown duration)
 - a. **Benzathine penicillin G** 2.4 million units IM once each week for three weeks. Patients who are receiving three doses of penicillin must restart their treatment if more than 10 days elapse since the last dose. They should also receive each dose no sooner than five days since the preceding one.

- b. For non-pregnant penicillin-allergic patients, **doxycycline** 100 mg orally twice daily for 30 days may be substituted.*

3. Neurosyphilis

- a. **Aqueous penicillin G** 3-4 million units IV q4h for 10-14 days.
- b. If there is a high suspicion for neurosyphilis and the patient is being referred elsewhere for lumbar puncture, we recommend giving **benzathine penicillin G** 2.4 million units IM once *before* the patient leaves clinic, in case she/he is lost to follow-up. This treats concomitant early syphilis and renders the patient noninfectious.
- c. For neurosyphilis that occurs in the setting of late syphilis or syphilis of unknown duration, **benzathine penicillin G** 2.4 million units IM weekly for 3 weeks should be administered after completion of neurosyphilis treatment.

4. Contacts/Clusters

- a. **Benzathine penicillin G** 2.4 million units IM once.
- b. **Doxycycline** 100 mg orally twice daily x 14 days for non-pregnant patients who are penicillin allergic or refuse penicillin.

Treatment may be given in the field by trained personnel.

*Notes: **Pregnant patients with syphilis require penicillin treatment. No other treatment should be given.** Pregnant women with a history of true penicillin allergy should be seen by the attending physician and referred for desensitization and treatment. The UCSF Immunology fellow should be paged to arrange evaluation.*

All patients should be alerted to the possibility of a Jarisch-Herxheimer reaction. This is characterized by flu-like symptoms that can be severe and are most likely to occur in primary and (especially) secondary syphilis, within hours after treatment. Patients should be told that this is not a drug allergy, but related to the death of the treponemes following treatment. In pregnant women this reaction may be associated with early labor, so consider admitting for inpatient observation if in the second or third trimester. Any pregnant woman treated for early syphilis as an outpatient should be advised to go to the emergency room if contractions occur.

Patients who are treated with doxycycline because of penicillin allergy or who refuse penicillin therapy should be cautioned regarding possible treatment failure and should be followed closely.

C. Follow-up

1. Early Syphilis

- a. Patients should have a repeat non-treponemal antibody test (VDRL or RPR) in 3 months, 6 months and 12 months after treatment. At all syphilis follow-up visits patients should be asked about any new neurological symptoms or symptoms that

might indicate a new infection. If patients have neurological symptoms, they should be evaluated and referred promptly.

- b. Pregnant patients should be evaluated monthly and should have a complete obstetric history documented at the initial visit to determine if there are other children who may have congenital syphilis. If this is a possibility, the City Clinic surveillance unit should be notified.
- c. If nontreponemal antibody titers have not declined fourfold by 12-18 months for secondary and early latent syphilis, or if they increase fourfold, the patient should be evaluated for re-infection or treatment failure and should be treated accordingly. Titers may decline more slowly in patients with HIV infection and those with prior cases of syphilis. The attending physician should be consulted for such cases.

2. Late Syphilis

- a. Patients should be seen by a clinician every week for three weeks if the patient is receiving penicillin therapy. All patients should be evaluated after the initial therapy to assess whether or not the patient had a Jarisch-Herxheimer reaction. A repeat non-treponemal antibody titer should be done at the second treatment. At follow-up visits, if titers increase fourfold, or an initially high titer ($> 1:32$) fails to decline after one year, or the patient has symptoms or signs attributable to syphilis, the patient should be evaluated for re-infection and neurosyphilis, and be re-treated. The attending physician should be consulted for such cases.
- b. Pregnant patients should be evaluated by a clinician during their weekly treatment visits, then monthly and should have a complete obstetric history to determine if they have other children who may need to be evaluated for congenital syphilis. Referral to the surveillance unit is indicated if other children are involved.

D. Counseling/Education

1. All early syphilis cases should be referred to a DCI for counseling and partner services. DCI should also be informed of cases of latent syphilis for which the nontreponemal antibody titer is $\geq 1:32$ (i.e. latent syphilis of unknown duration) so that the DCI can interview the patient as they would an early latent case.
2. Understand the importance of returning for follow-up treatment.
3. Be aware that the Jarisch-Herxheimer reaction may occur.
4. Return for follow-up serologic tests as indicated.
5. Refer sex partners(s) for examination and treatment.
6. Avoid sexual activity until 1 week after they and partner(s) complete all treatment.
7. Be screened for HIV and other STDs according to current clinic protocols.
8. Be offered condoms and advised that condoms can prevent future infections.

9. Be advised that syphilis is a marker of elevated HIV-risk. PrEP should be recommended to all patients with confirmed syphilis.

E. Evaluation and Treatment of Sex Partners

All sex partners of patients with early syphilis (or late syphilis with a nontreponemal antibody titer of $\geq 1:32$) should be evaluated clinically and should have a stat RPR and a lab based non-treponemal antibody test (VDRL or RPR). Contacts who are serofast, i.e., who have a known history of past treated syphilis and a persistently reactive RPR or VDRL titer, do not need to have a stat RPR performed. **For early syphilis, if the estimated exposure date(s) occurred within the preceding 90 days, the person may be infected yet seronegative; therefore, the person should be presumptively treated, regardless of reported sexual history or stat RPR result.** Contacts whose RPR is reactive should be diagnosed as having syphilis, staged, and be treated appropriately. If the sexual exposure of the contact occurred more than 90 days before the evaluation and the RPR is nonreactive, prophylactic treatment is not necessary. Contacts to patients with true late latent disease and who have a negative stat RPR need not be treated. We do not recommend routine treatment of an asymptomatic contact to an uninfected partner of a known syphilis case.

Syphilis partners/clusters should:

1. Be referred to a DCI for counseling and clustering.
2. Be aware that the Jarisch-Herxheimer reaction may occur.
3. Avoid sexual activity until 1 week after they and partner(s) complete all treatment.
4. Be offered condoms and advised that condoms can prevent future infections.
5. Be advised that syphilis is a marker of elevated HIV-risk. Individuals exposed to syphilis should be tested for syphilis and HIV, and PrEP should be recommended to all HIV-negative syphilis contacts.

Note: If there are any questions concerning any aspect of syphilis diagnosis, treatment, follow-up, LP, etc., ask the attending physician for advice. The City Clinic Clinician's line is available for telephone consult in difficult syphilis cases as well: (415) 487-5595.

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. Trichomoniasis is highly prevalent among women with HIV, but is rare in men who have sex with men. 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 membranes, preterm delivery and delivery of a low birth weight infant.

A. Diagnosis

1. History
 - a. Patients may be asymptomatic.
 - b. If symptomatic, patients typically present with a malodorous vaginal discharge, with or without vaginal or vulvar itching.
 - c. Men may present with symptoms of urethritis, epididymitis or prostatitis, 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. The cervix may have punctate hemorrhages (strawberry cervix).
3. Laboratory
 - a. Vaginal pH > 4.5 or normal.
 - b. Identification of motile trichomonads on a 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.
 - c. Vaginal swab for trichomoniasis NAAT (if available)
 - d. Culture using the InPouch TV culture system may be done for trichomonads in the SFCC on-site lab when the diagnosis is in question.
4. Diagnostic Criteria
 - a. Positive trichomoniasis NAAT **or**
 - b. 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 **or**
 - c. Identification of *T. vaginalis* by InPouch culture system **or**

- d. Trichomonads on liquid-based Pap.
- e. Since trichomonads die quickly, the sensitivity of wet mount is approximately 60%. Therefore, the diagnosis may have to be made on clinical grounds alone.

B. Treatment

Initial infection:

1. **Metronidazole** 2 g orally once *OR*
2. **Tinidazole** 2 g orally once (more costly) *OR*
3. **Metronidazole** 500 mg twice daily for 7 days*

****Note: Single dose regimen of metronidazole 2 g has been shown to be less effective than a one-week course in women with HIV, therefore HIV-positive women should be treated with a 7 day course of metronidazole 500 mg twice daily.***

Persistent infection/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.

1. If re-infection is likely, re-treat with primary regimens above.
2. Patients who fail to respond to single-dose therapy should be re-treated with
Metronidazole 500 mg orally twice daily for 7 days
3. Patients who fail with the 7-day therapy should be treated with
Metronidazole 2 g orally daily for 7 days or **tinidazole** 2 g orally for 7 days
4. Recalcitrant or possible metronidazole-resistant trichomonas infections (i.e., wet mount confirmed trichomoniasis after escalating dose regimens listed above) can have trichomoniasis confirmed by culture, using the InPouch culture system. Culture can be obtained from vaginal specimen or a spun urine sediment. Consultation and *T. vaginalis* susceptibility testing is available from CDC (tel: 404-718-4141).

Treatment in Pregnancy:

1. **Metronidazole** 2 g orally once can be used at any stage of pregnancy, but treatment of trichomoniasis during pregnancy has not been shown to reduce perinatal morbidity. The patient should be counseled that treating trichomoniasis might reduce symptoms and might decrease risk of respiratory or genital infection of the newborn, and that deferral of treatment until 37 weeks is an option. Tinidazole should not be used in pregnancy as the safety is unknown.

C. Follow-up

Re-test in 3 months.

D. Counseling/Education

Patients should:

1. Be counseled about the sexual transmission of trichomoniasis.
2. Understand how to take or use prescribed medications (e.g., alcohol should be avoided during and for 24 hours after treatment with metronidazole, or for 72 hours after treatment with tinidazole).
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for evaluation and treatment or provide them with patient-delivered partner therapy.
5. Know that males frequently are asymptomatic even if infected.
6. Avoid sex for at least 7 days after patient AND partner(s) are treated.
7. Be offered condoms and advised that condoms can prevent future infections.
8. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

Patient-delivered therapy should be given to all patients with *T. vaginalis* infections, with recommendation that partners also present for complete evaluation.

Urinary Tract Infections

Urinary tract infections (UTI) may be limited to the lower urinary tract (cystitis) or may include both the upper and lower tracts (pyelonephritis). The most common uropathogen is *Escherichia coli* (75-95%), followed by other species of Enterobacteriaceae, such as *Proteus mirabilis*, *Klebsiella pneumoniae*, and *Staphylococcus saprophyticus*. Uropathogens originate primarily from the bowel. Lower urinary tract infections appear to be limited to the mucosal surfaces of the lower urinary tract, which makes them relatively easy to cure with a short course of antimicrobial therapy. Symptoms generally include pain with urination, frequency, and urgency. These symptoms may occur from urethritis in the absence of bladder infection. Therefore, it is important to distinguish between urethritis (typically caused by gonorrhea or chlamydia) and cystitis, particularly in a sexually active population.

In young females, factors associated with increased risk of urinary tract infection include sexual intercourse, use of spermicide with or without diaphragm, history of a recent urinary tract infection and pregnancy. Most uncomplicated urinary tract infections in young females present with pain with urination, frequency, urgency, suprapubic pain and hematuria, but without fever or flank pain. Females with sexually transmitted urethritis often have milder symptoms of longer duration, may have cervical infection, and often a history of a new sexual partner.

Pyelonephritis is an upper urinary tract infection involving the kidney parenchyma. The infection usually ascends from the lower urinary tract and is characterized by fever, flank pain, chills as well as lower urinary tract symptoms. Nausea, vomiting and diarrhea are not uncommon. While uncomplicated pyelonephritis can be treated in the outpatient setting with close follow-up, hospitalization may be necessary for pregnant patients, and patients with nausea, vomiting, or lethargy.

A. Diagnosis

1. History

- a. Patients often present with acute onset (< 4 days) of pain with urination, urgency, and frequency. There may also be a history of hematuria.
- b. Patients should be carefully questioned regarding the presence of flank pain, nausea/vomiting, and fever or chills.
- c. Any history of chronic or recurrent UTIs or UTIs with a resistant organism as well as risk factors (e.g., pregnancy, diabetes, use of spermicide) should be elicited.
- d. Take a thorough sexual history because urethritis, vaginitis and cystitis can have a similar presentation. A recent new partner should raise suspicion of STD, and not necessarily a UTI, although UTIs can be associated with inadequate emptying of bladder and with intercourse (“honeymoon cystitis”).
- e. Older women may have more subtle or nonspecific symptoms when they have a UTI and warrant a more thorough evaluation.

2. Examination

- a. In young non-pregnant women with typical symptoms and the absence of vaginal symptoms, physical examination is often not necessary as long as the diagnosis is supported by laboratory findings (i.e. bacteriuria, pyuria).
- b. There may be suprapubic tenderness.
- c. A careful evaluation for flank (costovertebral angle) tenderness (CVAT) must be done. If present, take the patient's temperature.
- d. If vaginal symptoms are present, the presentation is atypical or the patient has a history of STDs, a pelvic exam should be performed to rule out vaginitis, cervicitis and PID.

3. Laboratory

- a. Vaginal swab for GC and CT NAAT.
- b. The patient should provide a clean catch urine specimen, to reduce the likelihood of contamination. The provider should explain the proper technique before sending the patient to the bathroom.
- c. Urine dipstick to assess for leukocyte esterase and nitrite.
- d. Urine microscopy to assess for number of WBC/HPF.

4. Diagnostic Criteria

- a. Positive leukocyte esterase and nitrite on a urine dipstick from a midstream clean catch urine in a patient with a compatible clinical presentation. The absence of leukocyte esterase substantially reduces the likelihood of cystitis, but false negative dipstick tests do occur, therefore examination of spun urine sediment is useful.
- b. The presence of > 10 WBCs per HPF from spun urine correlates with UTI. The presence of more than a few vaginal epithelial cells per high power field represents contamination and a poor urine collection. Repeat the clean catch urine collection before making diagnosis.
- c. Clinical symptoms (e.g., dysuria, urgency, frequency).
- d. Patient should be sent to his/her PCP or urgent care for urine culture and sensitivity if they do not respond to therapy, have pyelonephritis or recurrent infections.

B. Treatment

1. Uncomplicated Lower UTI (cystitis)

- a. May be treated with short course therapy.
- b. Does not require urine culture prior to treatment.

- c. Patients should follow-up if symptoms recur, persist, worsen and/or signs or symptoms of upper tract involvement occur.

Recommended (non-pregnant):

1. **Nitrofurantoin** (Macrobid) 100 mg orally twice daily for 5 days *OR*
2. **TMP-SMX SS** One tab orally twice daily for 3 days

Note: Nitrofurantoin should not be used if early pyelonephritis suspected due to poor absorption in renal parenchyma.

TMP/SMX should not be used if resistance prevalence is known to exceed 20% or if used for UTI in previous 3 months.

Alternate (non-pregnant):

Ciprofloxacin 250 mg orally twice daily for 3 days

Note: Fluoroquinolones such as ciprofloxacin should not be used in pregnancy.

Recommended (pregnant):

1. **Nitrofurantoin** (Macrobid) 100 mg orally twice daily for 5-7 days *OR*
 2. **Cefpodoxime** 100 mg orally twice daily for 3-7 days
2. Complicated Lower UTI

A lower UTI is considered “complicated” if any of the following are present:

- a. Recurrent infection within two weeks of completion of therapy.
- b. History of UTI with antibiotic-resistant organism.
- c. History of multiple serious antibiotic allergic reactions.
- d. History of multiple UTIs (> 5 UTIs, avoid TMP/SMX use).
- e. Male with UTI.
- f. Symptoms greater than 7 days.
- g. Pregnancy.
- h. Diabetes.
- i. Recent hospitalization or instrumentation.
- j. Other significant underlying medical conditions.

Treatment:

Must be tailored to patient history and presentation and typically requires a 7 day course of treatment – consult with the attending physician.

3. Upper UTI (pyelonephritis)

Notify attending physician and hospitalize for:

- a. Hemodynamically unstable (high pulse, low blood pressure).
- b. Pregnant.
- c. Vomiting and unable to tolerate oral meds or oral hydration.
- d. High fever, debility
- e. Unlikely to adhere to outpatient regimen, or to follow-up in clinic.

Patient-Delivered Partner Therapy (PDPT)

Effective clinical management of patients diagnosed with treatable STDs requires treatment of their sex partners as well. Current state law in California allows clinicians to provide additional courses of STD treatment for partners of patients.

Multiple studies have shown that sex partners who receive PDPT are more likely to get treated than are those who are notified of exposure but not given antibiotics or a prescription. There have been three randomized controlled clinical trials of heterosexual couples that demonstrate that PDPT reduces rates of repeat infection in the original patient. The CDC supports PDPT for heterosexuals with STDs. There are no randomized controlled trial data that show that PDPT decreases repeat infections for MSM, and PDPT may generate missed opportunities for diagnosis of HIV and syphilis in MSM who are not screening regularly for STDs. This concern has to be balanced against the need to quickly and efficiently treat exposed sex partners of MSM for bacterial STDs.

Patients diagnosed with the following STDs should be offered PDPT to give to all partners in the 60 days prior to diagnosis:

1. **Chlamydia**
2. **Gonorrhea***
3. **Nongonococcal urethritis (NGU)**
4. **Trichomonas**

In addition, at City Clinic, we consider PDPT for partners of patients with **PID** and **proctitis**.

**The recommended treatment regimen for gonorrhea includes an intramuscular injection of ceftriaxone, therefore partners of patients with gonorrhea should be strongly encouraged to come to clinic or see their primary care doctor for gonorrhea treatment. Providing a patient with gonorrhea a “partner pack” that includes an oral 3rd generation cephalosporin and azithromycin could be used as part of a harm reduction approach, if the patient’s sex partners are very unlikely to seek care.*

For current partners of patients with:

1. **Pubic lice**
2. **Scabies**

Optimally, a “partner pack” should be given to the patient for each partner. At City Clinic this includes:

1. Medication
2. Instructions for taking the medication
3. An information sheet about the STD for which they are receiving treatment
4. Condoms

5. Cards for City Clinic and InSpot, an online partner-notification resource.

Patients should always be encouraged to advise partners to present to a medical provider for a full evaluation, including assessment for other possible STDs. PDPT does not replace the need for this individual evaluation.

Events Requiring Attending Physician Notification

1. Patient must be sent to urgent care or the emergency department for further evaluation.
2. Pelvic examination cannot be conducted satisfactorily.
3. Uterine enlargement or pelvic masses are found on exam.
4. Acute salpingitis or acute abdomen in a pregnant patient.
5. First episode genital herpes is found in a pregnant woman.
6. Testicles are painful, tender, or enlarged.
7. The diagnosis is uncertain or disease is severe.
8. If any of the following diseases are suspected:
 - a. Pelvic actinomycosis
 - b. Resistant candidiasis
 - c. Chancroid
 - d. Epididymitis
 - e. Disseminated zoster
 - f. Presence of a bubo
 - g. Genital ulcer disease of uncertain etiology despite evaluation
 - h. Complicated syphilis cases including: syphilis in pregnancy, neurosyphilis, questions regarding syphilis staging or for assistance/confirmation of darkfield examinations
 - i. Gonorrhea treatment failure
 - j. Disseminated gonococcal infection (DGI)
 - k. Lymphogranuloma venereum (LGV)
 - l. Pelvic inflammatory disease (PID) not improved 72 hours after treatment
 - m. Complicated urinary tract infection (UTI) or pyelonephritis
9. The patient has a history of multiple drug allergies and requires treatment.
10. Serious sign of adverse reaction to treatment occurs, such as anaphylaxis (angioedema, urticaria, bronchospasm, hypotension, pruritis), skin rash, or anxiety.
11. Needed STD treatment or procedure is not specified in the preceding protocols (e.g., drainage of a bubo).
12. A serious surgical problem such as acute abdomen.

Common Medications Used for STDs

<u>Generic Name</u>	<u>Trade name</u>	<u>Category in Pregnancy</u>
Acyclovir	Zovirax	B
Amoxicillin	Amoxil	B
Azithromycin	Zithromax	B
Benzathine PCN G	Bicillin L-A	B
Cefixime	Suprax	B
Ceftriaxone	Rocephin	B
Cephalexin	Keflex	B
Ciprofloxacin	Cipro	C (avoid)
Clindamycin	Cleocin po	B
Clindamycin cream 2%	Cleocin	Avoid in pregnancy
Clotrimazole	Lotrimin	topical ok in pregnancy
Doxycycline	Doxy-caps (and others)	D (avoid)
Erythromycin	EES (and others)	B
Famciclovir	Famvir	B
Fluconazole	Diflucan	C (avoid)
Imiquimod	Aldara	Avoid in pregnancy
Levofloxacin	Levaquin	C (avoid)
Metronidazole	Flagyl	B (avoid in 1 st trimester)
Metronidazole gel	Metrogel	B
Miconazole	Monistat	B
Nitrofurantoin	Macrobid	B
Ofloxacin	Floxin	C (avoid)
Permethrin	Elimite	B
Podofilox	Podofilox	Avoid in pregnancy
Podophyllin (25%)	Podocon-25	Avoid in pregnancy
Tinidazole	Tindamax	C (avoid)
TMP-SMX	Septra	C (avoid)
Valacyclovir	Valtrex	B

Select STD Resources

- San Francisco City Clinic website: updated alerts, fact sheets, epidemiology reports and an electronic copy of clinical protocols:
<http://www.sfcityclinic.org> then click on providers
- California STD/HIV Prevention Training Center
<http://www.stdhivtraining.org/>
- CDC STD and guidelines:
<http://www.cdc.gov/std/>
<http://www.cdc.gov/std/treatment>
- National STD Curriculum
www.std.uw.edu