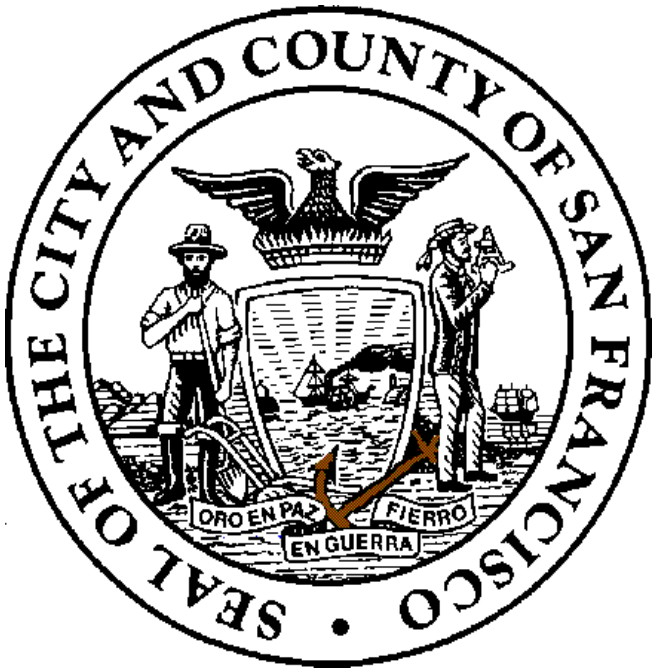
SAN FRANCISCO CITY CLINIC

CLINICAL PROTOCOLS

SEXUALLY TRANSMITTED INFECTIONS



Sexually Transmitted Diseases Prevention and Control Services

San Francisco Department of Public Health

San Francisco, California USA

August 2021

(*updated 2023 to include a chapter on mpox)*

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Foreword

This version of the San Francisco City Clinic STI Protocols was revised to incorporate many of the updates to the CDC STI Guidelines released in July 2021. In addition to replacing the term STD—sexually transmitted diseases— with STI—sexually transmitted infections—throughout the text, major changes have been made to the chapters on the treatment of gonorrhea, chlamydia, and NGU. This version was amended in 2023 to include a chapter on mpox, written by Drs. Franco Chevalier and Julia Janssen.

This edition of the guidelines uses gender neutral, anatomy-specific language whenever possible. When referring to data from studies that analyzed participants by male or female sex, including men who have sex with men (MSM), these identifiers have been retained.

Acknowledgments

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For expert consultation, please call (628) 217-6677 or visit our website at www.sfcityclinic.org.

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Actinomycosis in Persons with IUD

Actinomyces israelii is a fastidious, anaerobic Gram-positive bacterium that can colonize the pelvis of cisgender females and transgender males who have not undergone hysterectomy 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 patients, but evidence suggests that neither IUD removal nor antibiotic therapy is needed. If a patient's Pap smear shows actinomyces, they 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 they 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. Risk factors for BV include having multiple partners regardless of gender; partner concurrency; a new partner; condomless sex; douching, and HSV-2 seropositivity. BV occurs more often during menstruation, and in copper IUD users. Hormonal contraception has not been linked to an increased risk in BV. BV is rare among people who have not had sexual intercourse. Persons with BV may be at increased risk for other STIs (e.g., HIV, gonorrhea, chlamydia, and HSV-2). Treatment of cisgender male sex partners has not been beneficial in preventing BV recurrence. Treatment of cisgender female sex partners to prevent BV recurrence has not been studied, although studies have shown a high degree of concurrence between cisgender female partners with BV.

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 meet the clinical criteria on exam.
    c. Douching is associated with BV.
2. Examination
    a. Classically, BV produces a homogenous, malodorous, white or gray discharge that is adherent to the vaginal walls.
    b. In the absence of other conditions, the remainder of the exam is normal.
3. Laboratory

    BV can be diagnosed by clinical criteria (Amsel's) or by Gram stain (Nugent criteria).

    a. 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) Prevalence of clue cells on a saline preparation of vaginal secretions of at least 20%. Clue cells are epithelial cells with a granular, sand-like appearance and obscured edges caused by adherent bacteria.

b. Nugent criteria: Standardized 0–10-point score 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) seen on Gram stain.

c. Patients with proven or suspected BV should have a vaginal swab for trichomoniasis nucleic acid amplification test (NAAT). Also consider testing for GC, CT and M Gen, particularly if the patient has not been tested recently and has risk for acquisition of these infections.

B. Treatment

a. Non-pregnant patients

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

Recommended regimens:

1. **Metronidazole** 500 mg orally twice daily for 7 days *OR*
2. **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally at bedtime 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 72 hours 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 72 hours after use), *OR*
3. **Tinidazole** 2 g orally once daily for 2 days *OR*
4. **Tinidazole** 1 g orally once daily for 5 days *OR*
5. **Secnidazole** 2 g oral granules in a single dose (sprinkle oral granules onto unsweetened applesauce, yogurt, or pudding, and wash down with a glass of water if needed).

Additional regimens:

1. **Metronidazole** gel 1.3% (Nuvessa), one full applicator (5 g) intravaginally at bedtime in a single dose, *OR*
2. **Clindamycin** cream 2% (Clindesse), one full applicator (5 g) intravaginally at any time of day in a single dose (patients should be told that ovules are oil-based, and can weaken latex condoms and diaphragms for 72 hours after use)

b. Pregnant patients

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 patients can therefore be treated with either of the oral or vaginal regimens recommended for non-pregnant patients.

C. Follow-up

Routine follow-up is not recommended for non-pregnant patients. Recurrence is common (up to 30% of patients will have a recurrence within 3 months), and patients 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. CDC no longer recommends avoiding alcohol consumption while taking systemic metronidazole, as a review found no convincing evidence of a disulfiram-like interaction between alcohol and metronidazole.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refrain from using douches and other non-prescribed vaginal products.
4. Be offered condoms and advised that condoms may be helpful to reduce the frequency of recurrence.
5. Be screened for HIV and other STIs according to current clinic guidelines.
6. Studies do not support the use of any currently available intravaginal lactobacillus or other probiotics to treat BV or restore the normal vaginal microbiome. A clinical trial of a *L. crispatus* containing product (Lactin-V) has shown a reduction in BV recurrence, but this product is not yet FDA cleared.

E. Evaluation and Treatment of Sex Partners

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

F. Special Considerations Recurrent BV

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

For patients with multiple recurrences, as defined by more than three documented BV infections in a 12-month period, consider long term prophylaxis, after treating the current infection as indicated, with any of these regimens:

1. **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally at bedtime twice weekly for at least 3 months, *OR*
2. **Metronidazole** suppositories 750 mg, one intravaginally at bedtime twice weekly for at least 3 months, *OR*
3. **Metronidazole** or **tinidazole** 500 mg BID for 7 days, followed by **intravaginal boric acid** 600 mg daily for 21 days and suppressive 0.75% **metronidazole gel** twice weekly for 4-6 months. Boric acid is available from specialized compounding pharmacies, some commercial pharmacies, and online retailers.
4. **Metronidazole** 2 g orally plus **fluconazole** 150 mg orally once monthly for 6 months For

suppressive intravaginal metronidazole regimens, recurrence is common when treatment is discontinued. It is recommended to follow these regimens for 4-6 months. Oral combination therapy has been studied for up to 12 months.

Candida Balanitis

In persons with a penis, the glans 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, patients may exhibit shallow ulcerations on the glans. As in vulvovaginal candidiasis, 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 person who has *Candida vaginitis*, a person with a penis may experience transient erythema, burning, and pruritis on the glans. 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 persons and is more common in the setting of diabetes mellitus.

A. Diagnosis

1. History
    a. Rash on glans and/or prepuce.
    b. Often pruritic.
    c. More common in patients whose partners have recurrent vaginal candidiasis
    d. More common in patients 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 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:

1. **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 of the Vagina and Vulva

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. Persons who are immunosuppressed, diabetic, or pregnant are at greater risk for *Candida vaginitis*. Asymptomatic vaginal colonization with *C. albicans* is not uncommon and should not be treated.

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:

<u>Vaginal</u>:

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. **Butoconozole** 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 (extensive vulvar erythema, edema, excoriations, fissures) may be treated with Fluconazole 150 mg orally repeated in three days, or with a 7-14 day course of topical therapy.

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 candida 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 STIs 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 three 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 150 or 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):

1. **Fluconazole** 100 mg, 150 mg, or 200 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. Intravaginal boric acid capsules (600 mg intravaginally once daily for 3 weeks) may successfully treat these infections. 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); it still occurs in some regions of Africa, Asia, and the Caribbean.

A. Diagnosis

1. History
    a. Patients may present with a painful genital ulcer(s) on the penis, vulva, or vagina, and inguinal swelling or pain; dysuria, bleeding, or vaginal discharge are also seen. Vulvar or vaginal ulcer(s) 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 or by NAAT. These tests are not widely available (and at this time are not available at SF 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 recommended for 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 STIs 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 anogenital infection is one of the most common STIs in the United States. The single most important risk factor is young age. History of multiple partners, other STIs and past infection with chlamydia are other risk factors. An obligate intracellular bacterium, *Chlamydia trachomatis* (CT) can infect columnar epithelium of the urethra, cervix, rectum, and less commonly, the pharynx. Infections commonly occur without symptoms or signs, including in the penile urethra. Persons with a cervix may report urinary frequency and dysuria, an increase in vaginal discharge, or lower abdominal pain. Persons with a penis 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, endometritis, salpingitis, infertility, ectopic pregnancy, chronic pelvic pain and postpartum infection, 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. Symptoms of urethritis caused by CT may include dysuria, urethral irritation, and/or urethral discharge; typically, the symptoms tend to be milder than for gonococcal urethritis and in many cases (> 50%) may be asymptomatic.
    b. Rectal CT infections may be asymptomatic, or may resemble gonococcal proctitis with pain, bleeding, tenesmus or mucous discharge, particularly when caused by LGV-serovars of CT (see LGV).
    c. Cervical infections with CT may be asymptomatic. If symptomatic, patients may complain of vaginal discharge, urinary frequency and dysuria, or lower abdominal pain.
    d. For symptoms of complicated infections, refer to the epididymitis and PID protocols.
2. Examination
    a. Persons with urethral chlamydia may have a mucoid or purulent urethral discharge usually without inguinal adenopathy, although the exam may be normal.
    b. Persons with rectal chlamydia may have signs of proctitis, although the exam may be normal (see proctitis and LGV).
    c. Persons with cervical chlamydia may have evidence of cervicitis (mucopurulent cervical discharge, cervical erythema, edema, and friability), although the exam may be normal.

3. Laboratory and Screening

    a. A nucleic acid amplification test (NAAT) is the preferred screening test for genital or anal CT infection and can be performed from urine, vaginal, urethral, cervical, or rectal samples. In persons with a cervix, 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. Self-collected urine is the specimen of choice for diagnosing urethral chlamydia. Self-collected urethral meatal collection has been shown to be equivalent to self-collected urine or provider -collected urethral swabs in persons with a penis and could be offered if such patients prefer to self-collect a meatal swab or cannot produce a urine sample. FDA has approved the Aptima® NAAT platform for specimen collection at the rectum and pharynx. The SF Public Health Laboratory validated the Aptima Unisex and Multitest kits for patient self-collection at the rectum and pharynx.

    b. Real-time PCR using the Cepheid GeneXpert (GXP) is an alternative to NAAT for rapid molecular diagnosis of *Neisseria gonorrhea* and *Chlamydia trachomatis.* Results are available within 90 minutes of sample collection. FDA has approved GXP for diagnosis of GC and CT in urine, vaginal, endocervical, oropharyngeal, and rectal samples. SF City Clinic validated patient-collected rectal and oropharyngeal specimens as well. In the validation study, GXP was slightly less sensitive than NAAT testing for GC and CT, but still highly sensitive. See current clinic protocols for when to use NAAT vs GXP for detecting GC and CT at SFCC.

    c. 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. Persons 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.

    d. Diagnostic testing should be performed for all individuals with syndromes potentially caused by CT including urethritis, epididymitis, proctitis, vaginitis, cervicitis, PID, dysuria, pyuria and intermenses bleeding.

4. Diagnostic Criteria

    a. Positive test by NAAT or GXP of urine, cervical, vaginal, rectal, pharyngeal, or urethral specimens **or**

    b. A positive CT culture from the cervix, vagina, rectum, pharynx, or urethra (not routinely performed at SFCC).

B. Treatment

Increasing evidence suggests that doxycycline is superior to azithromycin for symptomatic CT urethritis, and doxycycline 100 mg BID x 7 days was shown to be superior to azithromycin 1 g for symptomatic and asymptomatic rectal CT in two randomized controlled trials of cisgender men who have sex with cisgender men (MSM). The prevalence of asymptomatic rectal CT infection is high in cisgender women with genital CT, even without reported anal intercourse, and thus it is important to treat cisgender women with genital CT with a regimen that is also effective for rectal CT. **For these reasons, doxycycline is now the recommended first-line regimen for all CT infections.** If there are significant adherence concerns or prior allergy or intolerance to doxycycline, azithromycin is the preferred regimen for CT. In addition, azithromycin remains the treatment of choice for pregnant persons with CT at any anatomic site.

a. Uncomplicated *Chlamydia* Infections*

Recommended regimens:

1. **Doxycycline** 100 mg orally twice a day for 7 days

Alternative regimens:

1. **Azithromycin** 1 g orally in a single dose *OR*
2. **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 doxycycycline 100 mg PO BID x 21 days. See sections on proctitis and LGV.

b. Chlamydia in Pregnancy

Doxycycline and levofloxacin are not recommended in pregnancy. Clinical experience and preliminary data support that azithromycin is safe and effective in pregnancy. All pregnant persons 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 persons:

1. **Amoxicillin** 500 mg orally three times a day for 7 days

C. Follow-up

1. Note that for up to 4 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 4 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 four weeks is only indicated in pregnancy. 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 randomized trial data showing that **azithromycin** is 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 in the following populations, since chlamydia is often asymptomatic:
    a. Cisgender women < 25 years who have sex with cisgender men (annual screening)
    b. Cisgender men and transgender persons, who have sex with cisgender men (screen every three months)
    c. Cisgender men age ≤ 30 years who have sex with cisgender women (annual screening recommended at SFCC, although not a national guideline)
8. Be screened for HIV and other STIs according to current clinic guidelines.
9. Be counseled about PrEP if at elevated risk for HIV-infection (note that PrEP should be recommended to cisgender men and transgender persons, who have sex with cisgender men, and 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 delivered partner therapy (PDPT) or field-delivered therapy may be treatment options for partners unlikely to come in for examination.

- **Cisgender male and transgender female partners** of person with *C. trachomatis* infection should receive PDPT with doxycycline 100 mg orally twice a day for 7 days.
- **Cisgender female and transgender male partners** of patients with *C. trachomatis* infections should receive PDPT with azithromycin 1 g orally once, unless they are unable to conceive, in which case they can receive doxycycline in the regimen above.

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*, *Neisseria gonorrhoeae* or *Mycoplasma genitalium* (usually occurring in cisgender 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 cisgender men over 35 years of age and may be associated with bladder outlet obstruction and resulting bacteriuria, often with the same enteric organisms associated with urinary tract infections (e.g., *E. coli*). Acute epididymitis caused by enteric organisms also occurs in cisgender men who have insertive anal sex. Data are lacking on epididymitis in transgender women; however, epididymitis should be considered in any transgender women with symptoms suspicious for epididymitis/orchitis. For the rest of this chapter, the word "patient" will refer to cisgender males, and transgender females who have not undergone orchiectomy. Symptoms and signs of acute epididymitis 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 patients, 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 patient 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, chlamydia, and M. gen NAAT tests should be done on all patients with epididymitis, as well as other STI screening as clinically indicated. If available, urine culture should be performed if epididymitis associated with bladder outlet obstruction is suspected.

4. Diagnostic Criteria

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

B. Treatment

Treatment should be initiated empirically when the patient presents for care, to prevent complications and decrease risk of onward transmission., and should be based on the risk for gonorrhea, chlamydia, or enteric organisms. Supportive treatment including analgesics, antipyretics, bed rest, sitz baths, and scrotal elevation should be instituted until tenderness has resolved.

1. **Acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms**

   (e.g patients ≤ 35 and patients who have insertive anal sex):

   Ceftriaxone* 500 mg IM once *AND* **levofloxacin**** 500 mg orally once daily for 10 days

2. **Acute epididymitis most likely caused by gonorrhea or chlamydia** (e.g. sexually active patients ≤ 35 who do not have insertive anal sex):

   Ceftriaxone* 500 mg IM once *AND* **doxycycline**** 100 mg orally twice daily for 10 days

3. **Acute epididymitis most likely caused by enteric organisms only** (e.g. patients who are not sexually active with other people or who are in a mutually monogamous relationship):

   Levofloxacin** 500 mg orally once daily 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.

*Use ceftriaxone 500 mg IM once for persons weighing <150 kg; use ceftriaxone 1 g IM once

for persons weighing ≥ 150 kg.

**If the M. gen NAAT is positive, levofloxacin (if given) should be stopped and the patient should receive doxycycline 100mg orally twice daily for 7 days, followed by moxifloxacin 400 mg orally once daily for 7 days.

4. 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. Bed rest, scrotal elevation, and NSAIDs may be provide additional symptomatic relief; symptoms may take several weeks after completion of antibiotics to fully resolve.

D. Counseling/Education

Patients with sexually transmitted acute epididymitis should:

1. Be counseled about epididymitis and its relationship to STIs.
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 STIs 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 STIs and empirically treated for chlamydial infections with doxycycline if not biologically capable of pregnancy or azithromycin if biologically capable of pregnancy and pregnancy has not been ruled out. 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, 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 11.9% among persons aged 14-29 years 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:

      i. **To confirm a clinical diagnosis of herpes**

      ii. **To distinguish between primary and recurrent disease**

      iii. **To guide counseling and prevention messages in patients with a partner with known genital HSV-2 infection**

   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.

   The results of HSV-2 antibody testing (HerpeSelect® HSV-2 EIA) are reported with an index value: ≤1 is negative, 1.1-3.0 is low positive, >3.5 is high positive. Index scores of 1.1-3.5 have a poor positive predictive value (PPV) of ~50%.
   Index values >3.5 are much more accurate (PPV ~90%). CDC recommends that all positive HSV-2 EIA results (but particularly those 1.1-3.5) should be confirmed with either an HSV-2 western blot (available at University of Washington) or a commercially available assay, (BioKit®), however these tests are not available at SFCC. Patients should be counseled about the risks of a false positive result before ordering the test.

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 Episode*:

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 STIs 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 an anogenital ulcer. For specifics regarding the management of a patient with an 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 (Southeast 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).

   k. Review the patient's history of previous STIs. If patient has a history of syphilis, determine the date(s) of prior treatment and treatment regimen, and date and titer of the last RPR (or VDRL).

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, lab-based RPR and clinician-ordered TPPA.
      (Per lab protocol, the TPPA is not run if the non-treponemal antibody test (RPR) is negative. The TPPA may be positive before the RPR, so it is important to ask the lab to run the TPPA regardless of the RPR result in suspected early cases).
   e. A point of care treponemal test (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. This test should only be used in patients who do not have a prior history of syphilis.

f. If the ulcer persists and syphilis and herpes are ruled out, consider evaluating the patient for LGV. Findings that would increase the likelihood of LGV include a positive Chlamydia NAAT from the urine or rectum, and a serpinginous shape to the ulcer, and inguinal lymphadenopathy or a soft, swollen mass along the shaft of the penis (local lymphadenitis called a bubonulus). LGV can also cause a painless ulcer at the site of inoculation and can be complicated by penile lymphangitis. If considering LGV as the etiology, consult with the attending physician. A swab of the ulcer should be collected using universal viral transport media to test for LGV.

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™ (point of care treponemal test) 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™ (point of care treponemal test) 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 lab 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 STIs 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. Individuals with vulvar, 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 STI 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-administered vs. patient-applied therapies, and should be chosen based on patient preference, availability of resources, and provider experience.

<u>Provider-Administered Therapies:</u>

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

Alternative Provider-Administered Therapies:

1. **Podophyllin resin 10% - 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.

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 cm^2 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 ($163.00/3.5 ml solution at Walgreens as of July 2021, but $35.17 at Walgreens with GoodRx coupon) 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 ($294/one month treatment (12 packets) at Walgreens as of July 2021, but $24.43 at Walgreens with GoodRx discount coupon) 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 anal dysplasia clinic at Zuckerberg San Francisco General (ZSFG). Referrals should be placed through e-referral. 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 that a person or their sex partner is having sex outside the relationship.
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 STIs 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 STIs as indicated and partners with a cervix 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 persons 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 persons 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 the penis 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. Persons with cervical GC may have abnormal vaginal discharge, abnormal bleeding, pelvic pain, or pain with urination, but as many as 50-70% of persons with cervical 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, and epididymitis and urethral stricture in the penis. Disseminated gonococcal infection (DGI) may occur regardless of gender but is not common. Untreated infection in pregnancy may result in premature delivery, including stillbirth. Newborns of persons with untreated cervical 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 the cervix, rectum, pharynx, and even the penile urethra can be asymptomatic. Persons 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. Conjunctivitis – Usually severe and rapidly progressive, with profuse purulent discharge and conjunctival edema that presents within 12 hours of exposure.

   f. 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, adenopathy (most have no signs of infection and when present are nonspecific).

   e. Conjunctivitis – profuse purulent discharge, conjunctival edema, lid swelling and tender preauricular adenopathy

   f. DGI – see section F below.

3. Laboratory and screening

   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 and extragenital gonorrhea infection and can be performed from urine, vaginal, urethral, cervical, oropharyngeal, and anorectal samples. In persons with a cervix, 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. FDA has approved the Aptima® NAAT platform for clinician collected specimens from the rectum and pharynx. Data support patient-collected specimens at these sites as being equal in performance to clinician-collected specimens. Pharyngeal screening is recommended for cisgender men, transgender men, and transgender women who perform fellatio, and rectal screening is recommended for cisgender men, transgender men, and transgender women who report receptive anal sex. See current clinic guidelines for specific recommendations regarding indications for pharyngeal and rectal GC screening, including in populations not mentioned above.

   c. Rapid RT-PCR using the Cepheid GeneXpert (GXP) is an alternative to NAAT for molecular diagnosis of *Neisseria gonorrhea* and *Chlamydia trachomatis*. Results are available in 90 minutes from the time clinical samples are loaded into the cycler. FDA has approved GXP for diagnosis of GC and CT in urine, and clinician collected vaginal, endocervical, oropharyngeal, and rectal swabs. SFCC validated the assay for patient collected vaginal, rectal, and oropharyngeal swabs. See current clinic protocols for when to use NAAT vs GXP for detecting GC and CT at SFCC.

4. Diagnostic Criteria

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

   b. Gram stain should be performed to evaluate all discharge from the rectum or urethra. The sensitivity of Gram stain of urethral discharge from the penis is near 95%. The endocervical Gram stain has a sensitivity of approximately 50%, and a specificity of 95%. A negative cervical or rectal Gram stain for gonorrhea should not be used to rule out infection at these sites. 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

1. Uncomplicated Cervicovaginal, Urethral, Rectal or Pharyngeal Infection

In 2015, to counter the threat of emerging cephalosporin resistance, CDC recommended dual therapy of GC with concomitant ceftriaxone and azithromycin. By 2020, however, no increases in ceftriaxone or cefixime MICs had been identified, and due to increasing prevalence of increased MICs of azithromycin in GC treatment, concerns about antibiotic stewardship related to the emergence of azithromycin resistance in other bacterial pathogens (including Shigella species, *Campylobacter jejuni*, and *Mycoplasma genitalium*), and evidence of inferior efficacy of azithromycin vs. doxycycline for the treatment of *Chlamydia trachomatis*, **dual therapy for GC with ceftriaxone and azithromycin is no longer recommended in the 2021 CDC guidelines**. As of December 2020, Ceftriaxone monotherapy is the only recommended treatment for GC in the United States, until additional anti-gonococcal antimicrobials are approved, or surveillance indicates rising MICs. Patients with GC in whom chlamydial infection has not been ruled out should receive anti-chlamydial therapy, usually in the form of doxycycline unless tetracyclines are contraindicated, in which case they should receive azithromycin.

<u>Recommended regimen:</u>

For patients weighing ≤ 150 kg (approximately 300 lbs):

Ceftriaxone 500 mg IM in a single dose

For patients weighing >150 kg:

Ceftriaxone 1 g IM in a single dose

For all patients (regardless of weight) in whom chlamydial infection has not been ruled out:

Give doxycycline 100 mg orally twice daily x 7 days as empiric co-treatment for chlamydia. In pregnant patients or for those in whom pregnancy has not been ruled-out, co-treat for chlamydia with azithromycin 1 g as a single dose instead of doxycycline.

Alternative regimen if Ceftriaxone unavailable:

Cefixime 800 mg orally once.

If chlamydia infection has not been ruled out, add **doxycycline 100mg orally twice daily x 7 days** (or azithromycin 1 g orally in a single dose if pregnancy has not been ruled out)

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

Alternative Regimen for Patients with Allergy

Should be reserved for individuals with uncomplicated cervicovaginal, urethral, or rectal infection and severe penicillin or cephalosporin allergy (defined as hives, angioedema, anaphylaxis or Stevens Johnson Syndrome/toxic epidermal necrolysis). There is no reliable alternative treatment for pharyngeal gonorrhea. If a thorough assessment of the allergy history identifies a severe reaction to ceftriaxone, consult with the attending physician.

Gentamicin* 240 mg IM in a single dose once and **azithromycin**** 2 g orally once

**Gentamicin use is cautioned during pregnancy because of risk for neonatal birth defects, nephrotoxicity, or ototoxicity.*

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

2. Treatment of gonococcal conjunctivitis

Patients with documented or suspected gonococcal conjunctivitis need urgent referral to ER or ophthalmology. Treatment, which should be initiated prior to departure from City Clinic, is **Ceftriaxone 1 g IM in a single dose**. Hospitalization for IV ceftriaxone is required in severe cases. Treatment typically includes a topical flouroquinolone and saline irrigation, along with daily monitoring until symptoms are improving.

3. Treatment of DGI

See section F below and call for expert consultation: (628) 217-6677.

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 should have a test of cure 14 days after treatment 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 screened for HIV, syphilis, and other STIs 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 cisgender men who have sex with men, transgender women, and transgender 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*.

Patient-delivered partner therapy (PDPT) with cefixime 800 mg orally once (and doxycycline 100 mg PO BID x 7 days if the index patient was treated for chlamydial coinfection) 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, and be screened for other STIs including HIV, but that if this is not feasible, they should take the patient-delivered partner therapy instead. Cisgender men should be strongly encouraged to refer cisgender female partners for clinician evaluation.

If the index patient has GC and CT, sex partners who are biologically capable of pregnancy should receive PDPT with cefixime 800 mg orally once and azithromycin 1 g orally once, as opposed to doxycycline.

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 doxycycline 100 mg orally twice daily x 7 days if chlamydial infection has not been ruled out) 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 an oral antibiotic 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 STIs

One of the most effective methods to prevent the acquisition of STIs is pre-exposure immunization. Currently licensed vaccines for the prevention of STIs 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 that 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. Persons with HIV
5. Persons experiencing homelessness

6. Travelers to endemic areas
7. 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, 2-6%% 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 STI 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. Heplisav-B is a newer, recombinant vaccine with a Toll-like receptor 9 adjuvant, that is more immunogenic than prior recombinant HBV vaccines and only requires 2 doses, one month apart.

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:

Heplisav-B (20 mcg) at 0 and 1 months. No need to restart or repeat does if missed or late

OR

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 persons, 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 licensed 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. HPV types 6 and 11 cause 90% of anogenital warts, and HPV types 16 and 18 account for 66% of all cervical cancers. The 9-valent vaccine protects against five additional HPV types that account for 15% of cervical cancers and is the only HPV vaccine currently distributed in the United States.

Gardasil-9 is indicated for the prevention of cervical cancer, anal cancer, and genital warts and is recommended for use in males and females aged 9-26 years. HPV vaccines are administered as a 2-dose series (months 0 and 6-12) for those who initiate vaccination before their 15th birthday. For those over age 15 and for immunocompromised persons, it is a 3-dose series (months 0, 1-2 and 6). People with a cervix 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, and for adults aged 27-45 based on shared clinical decision making between patient and provider. 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. Patients attending STI 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 patients attending STI clinics than among those attending family planning clinics. Moreover, studies conducted among patients attending STI clinics indicate that many do not understand the importance of Pap smears and almost half 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 patients with no history of an abnormal pap smear:

   a. Age < 21: Cervical cancer screening should be avoided.
   b. Age 21-29: Pap test every 3 years.
   c. Age ≥ 30-65: Pap test every three 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 at an STI screening visit, the health care provider should inquire about the result of the last Pap smear and should discuss the following information with the patient:

   a. Purpose and importance of a Pap smear.
   b. Whether a Pap smear was obtained during the clinic visit.
   c. 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.
   d. Patients who are experiencing homelessness and/or “out of the care loop” should have a Pap done on an STI 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 STI clinic.
   e. Note that as of February 2017, at City Clinic we are only able to offer pap smears to patients who have Family PACT or who are uninsured, San Francisco residents.

3. **Other Management Considerations**

   Other considerations in performing Pap smears are the following:

   a. 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).
   b. Liquid-based cytology can be performed during menstruation. Conventional cytology Pap test should be postponed if a patient is menstruating.

c. A patient with external genital warts does not need to have Pap smears more frequently than one without warts, unless otherwise indicated.

d. Patients who have had their cervix removed as part of a hysterectomy do not require annual Pap smears unless the hysterectomy was related to cervical cancer or its precursor lesions, or if the patient 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.

C. Colposcopy

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

D. Special Considerations Pregnancy

Pregnant patients should have a Pap smear as part of routine prenatal care. A cytobrush may be used for obtaining Pap smears in these patients, although care should be taken not to disrupt the mucous plug.

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is a sexually transmitted infection caused by serovars (sub-types) 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. LGV can also cause a painless ulcer at the site of inoculation and can be complicated by penile lymphangitis (bubonulus). Unlike mucosal infections caused by non-LGV serovars of *Chlamydia trachomatis*, LGV can induce a lyphoproliferative 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 cisgender men who have sex with cisgender men (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 swabs from the rectum, urethra, and genital ulcers. An LGV PCR can be run from a rectal or urethral swab collected in the Hologic Aptima Unisex kit or a universal viral transport kit. 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. If evaluating a genital ulcer for LGV, the swab should be collected using a universal viral transport kit.

   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. See also Appendix 1: Rectal symptoms protocol.

   e. Consult the attending physician for any cases of suspected non-rectal LGV.

B. Treatment*

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

1. **Azithromycin** 1 g orally every 7 days x 21 days may be effective, but clinical data are limited, *OR*

2. **Erythromycin** 500 mg orally four times daily for 21 days

*If LGV PCR cannot be done, 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

Patients with LGV should be advised to return to clinic if symptoms do not resolve. Longer courses of therapy may be required in the setting of invasive or complicated disease, e.g. if fistulas or buboes are present. All patients with treated for LGV should be retested for chlamydia approximately 3 months after treatment.

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 STIs according to current clinic protocols.
8. 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 SFCC, 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 STI 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 autoinoculation 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 STIs 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.

Mpox Diagnosis and Treatment at SFCC

In May 2022, mpox (formerly known an Monkeypox) emerged as a sexually transmissible infection among men who have sex with men (MSM) and transgender persons who have sex with men (TGSM) in countries that had not historically reported monkeypox (i.e., outside of previously designated endemic areas in West and Central Africa). In the United States, cases rose precipitously from May 2022 to a peak in late July 2022 before starting to taper off in August/September of 2022. Sexually transmitted mpox presents as a vesiculopustular rash, with or without constitutional symptoms, involving the anogenital region, face, trunk, and extremities. Lesions can often look similar in appearance to molluscum contagiosum (raised, pearly appearance, with dimple or pit in the center). The number of lesions can range from several to dozens or even hundreds. Most cases of mpox, while painful and upsetting, are mild to moderate and self-limiting. Painful proctitis, phimosis, and pharyngitis were prominent features of the 2022 outbreak in MSM. Severe, extensive disease requiring hospitalization and intensive care and sometimes resulting in death can occur, usually in immunocompromised persons, including people living with HIV with CD4 count < 350 cells/mm3.

The vaccine used for post-exposure prophylaxis and immunization during the 2022 outbreak (Jynneos) is an attenuated, live, replication-incompetent Modified Vaccinia Ankara (MVA) virus that is safe for use in immunocompromised persons, rather than the live, replication competent vaccinia virus used in the smallpox eradication campaign (Dryvax) or its modern equivalent (ACAM2000), which can cause symptomatic Vaccinia infection in vulnerable recipients or household contacts. Jynneos is given as a series of two doses administered 28-days apart. Peak immunity is reached 14 days after the second dose. The two-dose series reduces the risk of mpox infection by 66-89% and reduces the risk of severe disease and hospitalization in those who are infected. Childhood vaccination for smallpox or prior mpox infection offer protection against subsequent infection, but the degree and duration of protection are not yet defined, and reinfections have been reported.

Accurate testing using PCR of suspect skin lesions is available through San Francisco Public Health Lab and commercial labs with a turn-around time of 2-3 days. Treatment of suspected or confirmed cases includes supportive care, and antiviral treatment with tecovirimat (Tpoxx) for moderate to severe disease and for those at risk for complications (see Treatment section). Tecovirimat is available at SFCC or through the STOMP study under an EA-IND license held by the CDC.

A. Diagnosis

1. History

   The following characteristics should be ascertained during the history of present illness (HPI) when evaluating a patient with a rash or other symptoms concerning for mpox infection:

   a. History of exposure to a suspected, probable, or confirmed mpox case.

   b. Risk factors associated with exposure: intimate physical contact (including sexual contact) with people in a sexual network where mpox is spreading.

   c. Travel history.

d. HIV status and/or immunocompromising or other medical conditions that might indicate risk for severe mpox disease.

e. History of vaccination for mpox or smallpox.

f. Duration of rash.

Mpox can present with the following symptoms:

a. Fever, malaise, and body aches.

b. Distinctive rash or sores or spots that may appear as pimples or blisters on skin (anywhere in body), especially in genital region. Typical lesions progress through 4 stages—macular, papular, vesicular, pustular—before scab forms.

c. Umbilicated, indurated lesions.

d. Some people report pain or discomfort inside their rectum, rectal bleeding, and discharge.

2. Exam

   a. The following PPE is recommended when entering a room of a patient with suspected/known mpox: gown, gloves, eye protection, and N95 masks.

   b. Perform a thorough skin and mucosal (e.g., anal, vaginal, oral, nasal, ophthalmic) exam. Exam may reveal lesions that the patient may not be aware of or no cutaneous lesions at all.

   c. Spots may be red, flat spots which can then evolve to bumps. Bumps can be fluid filled with clear fluid which can then turn into pus. Pustules typically harden, then break and crust over into a scab. Scabs may be itchy.

   d. Lesions may be in different stages depending on timing of presentation.

   e. Assess for lymphadenopathy as it may be present (generalized or localized to several areas).

3. Laboratory

   a. Skin lesion material, including swabs of lesion surface, exudate, or lesion crusts are the recommended specimen types for laboratory testing of mpox virus specimens.

   b. Swab up to two lesions per patient, preferably from different locations on the body or from lesions that differ in appearance and place each swab in a separate viral transport tube.

   c. Vigorously swab each lesion, avoiding contamination of gloved hands, to ensure adequate viral DNA is collected. It is not necessary to unroof lesions to obtain an adequate sample. Please note that San Francisco Public Health Lab will not accept more than 2 lesions per patient.

   d. Order in Epic using “Orthopox/Mpox by PCR” indicating specimen site.

   e. Collect a rectal swab in persons with proctitis with or without visible lesions.

   f. Depending on appearance of lesions, consider also collecting a sample for darkfield microscopy and/or HSV PCR.

4. Diagnostic Criteria

    a. Presumptive diagnosis may be made by history and physical exam findings; however definitive diagnosis requires laboratory confirmation.

    b. Most cases are mild, but spectrum of disease ranges from mild to severe, and can be fatal. Disease severity depends on initial health of patient, immune response, prior vaccination status, comorbidities, route of exposure. Immunity from past vaccination may reduce intensity of clinical signs and symptoms.

        1) Mild: <25 lesions

        2) Moderate: 25-99 lesions

        3) Severe: 100-250 lesions

        4) Very severe: >250 lesions

        The CDC additionally defines severe disease as: large number of lesions that are confluent, hemorrhagic disease, necrotic lesions, severe lymphadenopathy that are necrotizing or causing obstruction (e.g., airways), sepsis, encephalitis, myocarditis, ocular or periorbital infections, pulmonary involvement with nodular lesions.

    c. People with HIV-associated immunosuppression, people with HIV who are not virologically suppressed, children (particularly <8 years of age), pregnant or breastfeeding women, immunocompromised people (malignancy, transplant recipients, autoimmune conditions), or those with chronic/acute chronic conditions are at increased risk of severe mpox.

B. Treatment

1. All patients with suspected or confirmed mpox should be treated with supportive care.

    a. Mild/Moderate disease:

        1) Acetaminophen and ibuprofen for mild pain.

        2) Salt-water rinses, antiseptic mouthwashes (e.g., chlorhexidine) and local anesthetics (e.g., viscous lidocaine) are recommended for oral lesions.

        3) Warm sitz baths and/or topical lidocaine for genital or anorectal lesions

        4) Topical corticosteroids may be used for genital lesions.

    b. Severe disease:

        1) Tramadol or morphine recommended for short-term management of severe pain (e.g., severe rectal pain secondary to proctitis).

        2) Neuropathic pain agents (e.g., gabapentin) have been used for short term management of pain in severe proctitis.

        3) Corticosteroid/local anesthetic suppositories or topical lidocaine gel may be used to relieve pain, spasm, and inflammation in proctitis.

2. Stool softeners may be considered to reduce pain associated with bowel movements (particularly if patient is on opioid analgesia.)
3. Treatment with anti-poxvirus agent tecovirimat (TPOXX) should be prioritized for people with severe disease, lesions in anatomic areas that might impede function or result in severe scarring or strictures (oropharynx, eye, penile foreskin, vulva, vagina, urethra, or rectum, anal lesions or painful lesions causing inability to handle secretions, urinate, or defecate) and people at risk for severe disease. Tecovirimat is FDA-approved for the treatment of human smallpox and is available for treatment of mpox under a CDC expanded access investigational new drug (EA-IND) protocol.
4. Although SFCC maintains a supply of tecovirimat, consider referring patients with confirmed or suspected mpox to the STOMP study prior to prescribing at SFCC. STOMP is a randomized trial examining the safety and efficacy of TPOXX for the treatment of mpox. Persons with mild-moderate mpox are randomized to TPOXX or placebo, and person with severe mpox are given TPOXX open-label. This trial is actively enrolling participants. If patient is interested, call 415-535-9495 or email ID-Research.ZSFG@ucsf.edu.
5. Prescribing tecovirimat at SFCC:
    a. Tecovirimat comes in 200 mg capsules and is dosed by weight (adult):
        1) 40-119 kg: 600 mg by mouth every 12 hours for 14 days
        2) > 120 kg: 600 mg by mouth every 8 hours for 14 days
    b. Under the EA-IND, the provider should obtain tecovirimat from the nursing station, affix a preprinted label with the dosing instructions and write in the patient's name, and dispense the bottles to the patient.
    c. Regulatory: For patients receiving tecovirimat from SFCC (i.e., not STOMP).
        1) Patient signs a paper informed consent, which is then scanned into their chart (by registration)
        2) Provider completes an electronic case report form for CDC available on the CDC mpox website. Supportive care should be offered to all persons with suspected or confirmed mpox, regardless of severity or tecovirimat use (see Treatment section).

C. Follow-up

1. Patient with suspected mpox infection should observe isolation precautions until infection is ruled out.
2. Those with confirmed mpox infection should remain isolated until all lesions have crusted, those crusts have separated, and a fresh layer of healthy skin has formed underneath.
3. If a patient with mpox cannot isolate (e.g., is at risk of losing their job or housing if they remain isolated) they must cover all lesions, wear a mask when around others, and avoid close bodily contact with others.
4. CDC Guidance as of 2023 is that having mpox infection likely confers some degree of

immune protection. Therefore, vaccination with Jynneos is not recommended for persons who have had mpox diagnosed since May 2022.
Exception: persons with immune compromise who acquire mpox infection may receive the 2-dose mpox vaccine series, and if they are diagnosed with mpox after their 1st dose, they may receive a 2nd dose.

D. Reporting to LINCS

The LINCS team will be automatically notified if the test results come back positive. Please notify LINCS@sfdph.org or Teams Chat Julia Janssen and Gloria Calero if you are seeing a patient with suspected mpox who you are sending to the ED.

E. Counseling / Education

1. People with mpox should remain isolated at home or at another location, to the extent possible, for the duration of the illness to minimize exposure to other potential contacts. Mpox is considered no longer transmissible once all lesions have fallen off and been replaced by new skin.
2. Avoid touching the face and eyes to prevent autoinoculation. Do not put in contact lenses. Involvement of the eyes can be a vision-threatening condition and should be treated urgently with antivirals and referred to ophthalmology.
3. Hand hygiene with use of alcohol-based hand rub or hand washing soap and water should be always performed by people with mpox and household contacts.
4. Cover lesions to prevent spread.
5. Notify sex partners from 4 days prior to symptom onset until date of isolation. Sex partners can receive PEP if eligible. Please notify patient that LINCS will reach out for partner services.
6. Patients diagnosed with mpox should consider condom use for 12 weeks, if planning pregnancy/fertility treatment, have immunocompromised partners, or are concerned about transmission to sex partner(s).
7. Mpox virus can be transmitted to the fetus during pregnancy or to the newborn by close contact during and after birth. Neonatal and pediatric mpox are potentially fatal.

F. Evaluation and Treatment of Sex Partners

1. Who is considered a close contact:
    a. Any sex contacts, including oral, anal, or vaginal sex, starting 4 days prior to patient symptom onset until date of isolation.
    b. Person who had direct contact with rash, scabs, saliva, or upper respiratory secretions (snot, mucus) of a person with mpox.
    c. Person who shared linens (clothing, sheets, or towels) that came into direct contact with mpox rash or lesions and were not washed.

2. Close contacts should:
    a. Check temperature BID, monitor for fever, chills, swollen lymph nodes, rash, and rectal symptoms for 21 days after last exposure.
    b. Consider post-exposure prophylaxis (PEP) if eligible. There is currently no test for asymptomatic mpox.
3. Close contacts are eligible for JYNNEOS as PEP if they: (1) are not fully vaccinated, (2) have no history of mpox, (3) are asymptomatic and (4) it is <14 days since exposure. JYNNEOS should be offered as soon as possible as it is thought to be most effective if given within 4 days (and up to 14 days) after exposure to prevent infection or attenuate disease if infected. Sex partners/contacts who are fully vaccinated or have a history of mpox do not need additional vaccine doses (if someone is immunocompromised, has a history of mpox and is not fully vaccinated, PEP may be given). Anyone who is symptomatic should first be evaluated by a provider. If it has been more than 14 days, JYNNEOS can be recommended as pre-exposure prophylaxis. If a child <6 months is a close contact, please consult with Julia Janssen and Stephanie Cohen prior to recommending JYNNEOS as PEP.

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* (M. gen) 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 mucopus. 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 inserted into the 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 and M. gen NAAT.

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

Treatment should be determined based on the results of diagnostic testing. Adolescents, patients unlikely to return for treatment, and persons 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:

Doxycycline 100 mg orally twice daily for 7 days

Note: Doxycycline is contraindicated during pregnancy and lactation; azithromycin 1 g orally should be used for pregnant or lactating patients, and patients in whom pregnancy cannot be ruled out or who are not on a highly effective form of birth control, such as an IUD, implant, or tubal ligation. When in doubt, obtain a negative urine pregnancy test before giving doxycycline.

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.

If the M. gen NAAT is positive and treatment had been previously initiated with doxycycline, the patient should complete 7 days of doxycycline followed by **moxifloxacin** 400 mg orally x 7 days

C. Follow-up

1. If symptoms persist, patients 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 STIs according to current clinic protocols.

E. Evaluation and Treatment of Sex Partners

Cisgender men who are sex partners in the past 60 days of patients with MPC should be examined for STIs and treated with the same regimen.

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

Mycoplasma Genitalium

Mycoplasma genitalium (M. gen) was first isolated in 1980 and is now recognized as one of the most common causes of penile urethritis, responsible for 15-20% of non-gonococcal urethritis (NGU) cases, 20-25% of non-chlamydial NGU, and 40% of persistent or recurrent NGU. M. gen is identified in 10-30% of cervicitis cases and up to 22% of PID cases. M. gen is commonly identified in the rectum in cisgender men who have sex with cisgender men, but its pathogenic role at this site is not fully understood. Persons with cervical M. gen infection may report urinary frequency and dysuria, an increase in vaginal discharge, inter-menstrual or post-coital bleeding, or lower abdominal pain. Persons with M. gen infection of the penile urethra may have symptoms that include urethral itch, dysuria, or a mucoid-to-purulent discharge. Serious complications potentially related to M. gen include epididymitis, endometritis, salpingitis, infertility, preterm delivery, and chronic pelvic pain. However, a causal relationship between M. gen and these complications has not been established, as there are few prospective studies, and the data are inconsistent. Sexually acquired reactive arthritis has also been described. While asymptomatic genital infections are common, there are not data to suggest that screening asymptomatic patients decreases complications, and thus at this time, testing is reserved for symptomatic patients and partners of patients diagnosed with M. gen. M. gen is a small, slow growing organism and is extremely difficult to grow in culture. A NAAT test for M. gen was approved by the US FDA in January 2019. Treatment of M. gen can be difficult. Doxycycline results in cure in <40% of cases. Resistance to azithromycin monotherapy, which can be induced during treatment, is rapidly growing. Resistance to moxifloxacin monotherapy has been observed. Sequential therapy, with doxycycline followed by either moxifloxacin or azithromycin, results in a higher cure rate and less resistance, presumably by reducing bacterial load with doxycycline before definitive treatment with the second antibiotic. Macrolide susceptibility testing for M. gen, which is not yet available in the United States, allows selection of azithromycin or moxifloxacin based on sensitivities of a patient's M. gen strain.

A. Diagnosis

1. History
    a. Persons with a penis may report dysuria and/or urethral discharge. Typically, the symptoms are milder than for gonococcal urethritis.
    b. Persons with a cervix may report vaginal discharge, urinary frequency and dysuria, lower abdominal pain, or inter-menstrual or post-coital bleeding.
    c. For symptoms of complicated infections, refer to the epididymitis and PID protocols.
2. Examination
    a. Persons with penile urethral M. gen infection may present with mucoid or purulent urethral discharge usually without inguinal adenopathy.
    b. Persons with M. gen infection in the cervix may present with mucopurulent cervical discharge, cervical erythema, edema, friability, or increased vaginal discharge.

3. Laboratory

    a. A nucleic acid amplification test (NAAT) is the preferred test for M. gen infection and can be performed from a urine sample or urethral, meatal, endocervical, or vaginal swab.

    b. Diagnostic testing should be performed for all individuals with syndromes potentially caused by M. gen including urethritis, epididymitis, vaginitis, cervicitis, PID, dysuria, pyuria and inter-menstrual or postcoital bleeding.

4. Diagnostic Criteria

    a. Positive NAAT test for M. gen from urine or vaginal swab.

B. Treatment

1. Initial Infections:

Recommended regimen:

a. If macrolide resistance testing is **not** available:

Doxycycline 100 mg twice daily for 7 days, followed by moxifloxacin 400 mg orally daily for 7 days (14 days in the setting of PID)

b. If macrolide resistance testing is available AND the organism is **macrolide susceptible**:

Doxycycline 100 mg orally twice daily, then azithromycin 1 g orally once, followed by 500 mg orally daily x 3 days (2.5 g total)

c. If macrolide resistance testing is available AND the organism is **macrolide resistant**:

Doxycycline 100 mg orally twice daily, then moxifloxacin 400 mg once daily for 7 days (14 days in the setting of PID)

2. Persistent infection/treatment failure

Macrolide resistance is common in M. gen and resistance to fluoroquinolones is rapidly emerging. Patients with M. gen who undergo treatment with moxifloxacin (or azithromycin) and return with signs and/or symptoms of persistent NGU or cervicitis, should be re-tested for M. gen. Ideally, re-testing occurs > 3 weeks after treatment as false positives are possible. Patients initially treated with moxifloxacin can be treated with extended-dose azithromycin (1 g orally x 1, then 500 mg orally daily x 3 days) while awaiting repeat test results. Additionally, the attending physician should be alerted about the concern for M. gen treatment failure. If M. gen resistance testing is available, treatment should be guided by results of resistance tests. For repeat positive tests, options include:

Minocycline 100 mg orally twice daily x 14 days

Pristinamycin 1 g 4x daily for 10 days (requires compassionate use approval by FDA or coordination with Dr. William Geisler at UAB)

Lefamulin (not currently available, dosage TBD)

C. Follow-up

Note that for 3 weeks after completion of therapy, nonculture tests (e.g., NAATs) may detect biologically inactive *M. genitalium* DNA and may yield false-positive results. Routine tests-of-cure or rescreening in asymptomatic persons are not recommended.

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. Patient-delivered partner therapy is not recommended at this time for M. gen. Partners should be tested and treated based on test results.
4. Abstain from sex until partner(s) have been tested and completed therapy (if partner(s) are also positive).
5. Be offered condoms and advised that condoms can prevent future infections.
6. Be screened for HIV and other STIs according to current clinic guidelines.
7. 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 M. gen infection should be examined, tested, and treated only if test results are positive. Patient-delivered partner therapy is not recommended at this time for M. gen. If it is not possible to test the partner, the antimicrobial regimen used to treat the index patient could be offered to the partner

Patients should be instructed to refrain from having sex until after treatment is completed and should not resume sexual activity with their partner until after the partner completes treatment.

<u>For receptive anal sex partners of men with M. gen urethritis</u>:

Data are limited on how common rectal M. gen is among the receptive anal sex partners of men with M. gen urethritis. Whether rectal M. gen infection causes symptomatic rectal disease (i.e. proctitis) is unclear. It is possible that rectal M. gen infection could lead to repeat urethral infection in the insertive sex partner.

Currently, there is no commercially validated M. gen test for rectal specimens, and the optimal management strategy for receptive anal sex partners of male patients with M. gen urethritis is unclear. Partners should be counseled on risks and benefits of pursuing empiric treatment for possible asymptomatic rectal M. gen. If they opt for treatment, we recommend doxycycline 100 mg orally twice daily x 7 days followed by moxifloxacin 400 mg orally daily x 7 days for empiric treatment of asymptomatic rectal M. gen infection.

Nongonococcal Urethritis

Nongonococcal urethritis (NGU) is inflammation of the urethra caused by pathogens other than gonorrhea. Pathogens that cause NGU can be transmitted through oral, anal, and vaginal sex.

Symptoms of nongonococcal urethritis (NGU) may include dysuria, a mucoid, mucopurulent, or purulent urethral discharge, or urethral pruritis in persons with a penis. 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 persons.

Complications of CT-associated NGU include epididymitis, prostatitis and reactive arthritis. *Mycoplasma genitalium* (M.gen) is another frequent cause of NGU (10-25% of cases). Enteric bacteria can cause NGU in persons who have insertive anal sex. Other less common causes of NGU include *Trichomonas vaginalis* (in persons with a penis who have vaginal sex), HSV types 1 and 2, Epstein Barr Virus, and adenovirus. *Haemophilus influenzae* has also been identified as a possible causative agent, particularly in MSM who practice insertive oral sex. Therefore, it is possible, though not common, that a patient in a monogamous relationship may develop NGU due to receiving oral sex from their partner. There is debate about whether Ureaplasma species cause urethritis. Other potential etiologies include undetected infectious rectal or vaginal pathogens, a transient reactive dysbiosis after exposure to a new microbiome, or a noninfectious reactive etiology. A microbiologic diagnosis may remain elusive in 20-50% of cases of urethritis. 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. CDC suggests inserting a swab into the urethral meatus so that it contacts the urethral wall, to collect secretions for Gram stain, but this is not standard practice at SFCC.

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, gonorrhea, and M. gen.

   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.

   NGU is confirmed in symptomatic men when urethritis criteria are met and there is either no discharge on exam or the gram stain does not contain gram-negative intracellular diplococci.

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 patients 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.

Increasing evidence suggests that doxycycline is superior to azithromycin for chlamydial NGU. In addition, because macrolide resistance is common among M. gen and induced during treatment with azithromycin, it is preferable *not* to use single-dose azithromycin empirically in clinical syndromes, such as NGU, in which M. gen is prevalent. Therefore, doxycycline is now the recommended first-line empiric regimen for NGU. The full course of medication should be provided in the clinic or health care provider's office and the first dose should be administered in the clinic. If there are significant adherence concerns or prior allergy or intolerance to doxycycline, azithromycin is the preferred alternative regimen. Note, however, that a multiday dosing strategy of azithromycin is now favored over a single 1 g dose, as pharmacokinetic data suggest this may reduce the induction of macrolide resistance during treatment.

Recommended regimens:

1. **Doxycycline** 100 mg orally twice daily for 7 days

Alternative regimens:

1. **Multi-day azithromycin regimen*:**
    A. **Azithromycin** 1 g orally on day 1, followed by 500 mg daily x 3 days (2.5 g total) *OR*
    B. **Azithromycin** 500 mg orally on day 1, followed by 250 mg daily x 4 days (1.5 g total)

    *****Note regimen (a) is approved for M. gen and is preferred at SFCC if using a multi-day azithromycin regimen to treat NGU
2. **Azithromycin** 1 g orally in a single dose (if multi-day regimen not available or not able to be tolerated by patient)

If the M. gen NAAT is positive:

1. If the patient was treated with doxycycline, the patient should be treated with moxifloxacin 400 mg orally daily for 7 days immediately after completing the 7 days of doxycycline (sequential therapy for M. gen, which also treats chlamydia if coinfected).
2. If the patient was treated with azithromycin (single or multi-dose), advise patient to return to clinic if symptoms not resolved by day 7. In that scenario, confirm persistent NGU by microscopy and if persistent, treat for M. gen with sequential therapy (doxycycline 100 mg orally twice daily x 7 days followed by moxifloxacin 400 mg orally daily x 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, CT or trichomonas urethritis should return in 3 months for repeat testing for these organisms, since these individuals are at high-risk for repeat infection. At this time, repeat testing for M. Gen after treatment is completed is not recommended unless the patient is symptomatic.

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. For M. gen, we recommend abstaining from sex for 7 days *following the end of treatment*.
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 STIs according to current clinic protocols.
8. Be counseled about PrEP if at elevated risk for HIV-infection.

E. Evaluation and Treatment of Sex Partners

1. 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.
2. 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. For patients with confirmed M. gen, we recommend abstaining from sex for 7 days *following the end of treatment*.
3. 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.
4. Patient delivered partner therapy (PDPT) can be provided if the patient thinks it is unlikely their partners will seek evaluation. These PDPT regimens can be dispensed at the time of the NGU diagnosis (while microbiologic tests are pending). <u>The patient should be counseled to follow-up their test result, and to inform their partner if a specific microbiologic etiology is confirmed</u>. If the patient tests positive for M. gen, their partner will need to come into the clinic for evaluation and management, as SFCC does not provide PDPT for M. gen.

   PDPT Regimens Offered to Patients with NGU:

   a. <u>For partner with a vagina:</u> Azithromycin 1 g orally in a single dose

   A. <u>For partners with a penis:</u> Doxycycline 100 mg orally twice daily for 7 days

SFCC does not currently offer PDPT for patient diagnosed with M. gen but recommends that partners of patients treated for M. gen come in for evaluation as contacts (see *Mycoplasma genitalium* protocol).

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 (i.e. urethral symptoms that persist after completing a course of treatment for NGU) 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*(M. gen) in persons who were not tested for *M. genitalium* initially. *Trichomonas vaginalis* may cause urethritis in persons with a penis who have sex with persons with a vagina. NGU can be associated with receiving fellatio; 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. If the patient has not been previously tested for M. gen, send a urine M. gen NAAT test.
4. For persons with a penis who have sex with persons with a vagina, send a urine trichomoniasis NAAT test.

B. Treatment

If the patient has persistent urethritis and is believed to have correctly completed a recommended regimen, has had their partner(s) treated appropriately, and denies re-exposure, the following approach is recommended (assuming infection with *Neisseria gonorrhea* has been ruled out):

1. If M. gen testing is not available, make sure patient has completed doxycycline 100mg orally twice daily for 7 days, then add treatment with moxifloxacin 400 mg orally daily for 7 days.
2. If M. gen testing is available but the patient has not been previously tested for M. gen, send a urine M. gen NAAT test and, if the patient is agreeable, defer treatment until test results are back. If the M. gen NAAT is positive, treat with doxycycline 100mg twice daily for 7 days, followed by moxifloxacin 400 mg orally daily for 7 days.
3. If the patient is already known to be M. gen negative and was treated with **doxycycline** originally, treat with **azithromycin** 1 g orally once.

4. If the patient is already known to be M. gen negative and was treated with **azithromycin** originally, treat with **doxycycline** 100 mg orally twice daily for 7 days.
5. If the patient has been treated with doxycycline and azithromycin and is negative for M. gen, Chlamydia, gonorrhea, trichomoniasis and HSV, withhold additional antibiotic treatment and consider referral to urology. In areas with high prevalence of Trichomoniasis (and if trichomoniasis NAAT testing is unavailable), add the following medication for persons with a penis who have sex with persons with a vagina:

    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.
6. 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 (for M. gen, we recommend abstaining from sex for 7 days *following the end of treatment)*.
5. Be offered condoms and advised that condoms can prevent future infections.
6. Be screened for HIV and other STIs 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 partners with a vagina 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 and a trichomoniasis NAAT in cisgender female and, if they have a vagina, transgender male partners of 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 influenza*, *Gardenerella vaginalis*, enteric Gram-negative rods, anaerobes including *B. fragilis, 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 persons with PID have no symptoms, nonspecific symptoms (dysparenunia, abnormal vaginal bleeding, vaginal discharge) or just mild-to-moderate lower abdominal pain and tenderness; indeed, many persons 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 poor descriptors since PID reflects the site(s) of infection, not the degree of symptomatology. As stated above, persons 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 they appear to be clinically stable, are reliable and do 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 persons 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, including abnormal bleeding, 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 or masses.
    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 swab for GC and CT NAAT
    e. Vaginal swab for trichomoniasis NAAT
    f. Vaginal swab or urine for M. gen NAAT
    g. Test for syphilis and HIV
    h. 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 persons at risk for STIs, especially young, sexually active persons assigned female sex at birth, 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, C. trachomatis, or M. genitalium*

Other diagnostic criteria (not available at City Clinic):

a. Elevated erythrocyte sedimentation rate (ESR) or c-reactive protein (CRP).

b. Histopathologic evidence of endometritis on endometrial biopsy.

c. Characteristic findings with transvaginal sonography, CT, MRI, or during laparoscopy.

B. Treatment

Outpatient treatment is standard in those patients with mild to moderate symptoms, able to tolerate the medications, and willing to return for reassessment. Regimens to treat PID should be reliably effective against gonorrhea and chlamydia, as the patient may have upper tract disease that is not captured by endocervical screening, and should cover anaerobes, such as *B. fragilis*, as well. There is evidence that the addition of metronidazole to outpatient PID treatment regimens more effectively clears anaerobes from the endometrium and is no less tolerable than regimens that do not include metronidazole, therefore the addition of metronidazole to outpatient treatment of PID is recommended regardless of the evidence for BV on wet mount of vaginal secretions.

All patients who begin outpatient treatment should be clinically re-evaluated within 72 hours, including a bimanual exam for cervical motion and adnexal tenderness, and if not improved should start parenteral therapy on either an outpatient or inpatient basis.

a. <u>Regimen A</u>

Ceftriaxone 500 mg IM once *AND*

Doxycycline 100 mg orally twice daily for 14 days PLUS,

Metronidazole 500 mg orally twice daily for 14 days

b. <u>Regimen B (not available at City Clinic)</u>

Cefoxitin 2 g IM once *AND* **Probenecid** 1 g orally once *AND*

Doxycycline 100 mg orally twice daily for 14 days PLUS

Metronidazole 500 mg orally twice daily for 14 days

c. <u>Notes on PID regimens:</u>

1) Use ceftriaxone 500 mg IM once for patients weighing < 150 kg
use ceftriaxone 1g IM once for patients weighing ≥ 150 kg.

2) If the patient's M. gen NAAT is positive, doxycycline should be given for 7 days followed by moxifloxacin 400 mg orally daily for 14 days. The optimal treatment of M. gen in the setting of PID has not been established; however, infections have been

successfully eradicated with moxifloxacin 400mg orally once daily for 14 days. Moxifloxacin will also cover CT, if concurrent CT is identified.

3) Metronidazole should be included in the PID treatment regimen, regardless of evidence for BV mount.

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

d. Alternative Oral Regimens with Quinolones for patients with severe allergy to 3rd generation cephalosporins

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 (e.g., severe allergy to 3rd generation cephalosporins) the following can be used if the risk of GC is low:

Levofloxacin 500 mg once daily for 14 days *OR* **Moxifloxacin** 400 mg once daily for 14 days

WITH

Metronidazole 500 mg orally twice daily x 14 days

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.

e. Hospitalization is recommended in the following situations: *

1) Surgical emergencies such as appendicitis or ectopic pregnancy cannot be excluded.

2) A pelvic abscess is suspected.

3) The patient is pregnant.

4) Patient compliance is uncertain.

5) Severe illness precludes outpatient management (e.g., temp > 38.3°C, moderate or severe dehydration, vomiting, peritoneal signs present).

6) 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 they were diagnosed).

Follow-up at three days should establish:

1. Patient adherence to medications.
2. Defervescence (if initially febrile)
3. Symptomatic improvement.
4. Clinical improvement in adnexal, cervical motion, and uterine tenderness as documented by a repeat bimanual examination, and abdominal tenderness (direct and rebound).

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 60 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. If diagnosed with chlamydial or gonococcal PID, 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 800 mg orally once and doxycycline 100 mg orally BID x 7 days 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 doxycycline) and be screened for other STIs.

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 persons diagnosed with PID. In compliant patients with uncomplicated PID, the IUD may be left in place during antimicrobial treatment if the patient 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. *M. genitalium* has been identified in some cases of proctitis but there is debate as to whether it is causative. Inflammatory STIs such as CT or GC and ulcerative STIs 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) and PrEP should be recommended.

A. Diagnosis

1. History
    a. Patients present with symptoms referable to the rectum: rectal pain, irritation, tenesmus, or discharge.
    b. Patients will typically have a remote or recent history of receptive oral-anal, digital-anal, or penile-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 chlamydia and gonococcal NAAT.
    c. Obtain a rectal swab for reflex LGV testing, performed by the SFDPH Public Health Lab if the rectal Chlamydia NAAT is positive (see LGV). As of July 2021, the LGV PCR can be run at SFDPH PHL from a rectal swab collected in viral transport media or using the Aptima unisex collection kit.

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).

g. See Appendix 1: Rectal symptoms protocol for additional detail

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

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

Consider adding **Acyclovir** 400 mg orally three times daily or **valacyclovir** 1 g twice daily or **famciclovir** 250 mg three times a day for 7-10 days for HSV infection

If there is a high suspicion for LGV infection (≥ 10 WBCs on gram stain of rectal discharge, bloody discharge, perianal or mucosal ulcers or tenesmus) use the following regimen:

Ceftriaxone* 500 mg IM in a single dose once and **doxycycline** 100 mg orally twice daily x 21 days**

*Use ceftriaxone 500 mg IM once for patients weighing <150 kg; use ceftriaxone 1 g IM once for patients weighing ≥ 150 kg.

**If the patient is empirically treated for LGV and the rectal CT NAAT is negative, the doxycycline can be discontinued after 7 days. See Appendix 1: Rectal symptoms protocol for additional details.

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. For patients with persistent symptoms after standard treatment for proctitis, consider empiric therapy for *M. genitalium* (see *M. genitalium* chapter) or, if validated, rectal NAAT for *M. genitalium* and treat if detected.

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 STIs according to current clinic guidelines.
7. In addition, PrEP should be recommended to all HIV-negative MSM and trans patients with confirmed proctitis, and all patients with proctitis should be tested for HIV and counseled about PrEP.

E. Evaluation and Treatment of Sex Partners

Sex partners in the past 60 days of patients with proctitis should be:

1. Given patient-delivered partner therapy for gonorrhea and chlamydia with:

   Cefixime 800 mg orally once and **Doxycycline** 100 mg orally twice daily for 7 days

2. 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. Patients 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 STI 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. Therefore, patients should 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 STIs 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 STIs 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. Specialty 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. Latent syphilis is further classified as early latent (duration of less than one year) and late latent syphilis (duration of more than one year). Latent syphilis of unknown duration refers to persons with late latent syphilis who have a nontreponemal titer of ≥ 1:32. They should be managed clinically as late latent syphilis but offered partner services as for early latent syphilis.

Tertiary syphilis includes cardiovascular syphilis (thoracic aortic aneurysm, aortic valve disease), late 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. Manifestations of early neurologic syphilis usually occur within the first months or years after infection and include ocular syphilis, otosyphilis, meningitis, cranial nerve dysfunction, stroke, meningovascular syphilis, and acute altered mental status. Manifestations of late neurologic syphilis include general paresis (dementia, bizarre behavior, psychosis) and tabes dorsalis (shooting pains, gait disturbance, Argyll-Robinson pupils). Ocular syphilis and otosyphilis can also occur as a late manifestation of neurologic syphilis.

Syphilis in Special Populations

People living with HIV:

Unusual serologic responses have been observed among people living with HIV 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 people who are biologically capable of pregnancy with syphilis. **All people who could become pregnant diagnosed with any stage of syphilis must have a stat urine pregnancy test.** If the test is positive, they must be counseled concerning syphilis, pregnancy, and risk to the fetus. They should be treated with penicillin as indicated by stage of infection and a prenatal care appointment should be made for them. Pregnant people 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 people 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 people living with HIV.
    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 SFDPH 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, or those who are serofast, unless a quantitative stat RPR can be performed to distinguish a new infection from their serofast baseline.

d. Both a nontreponemal test (RPR or VDRL) ***and*** treponemal test (TPPA) should be performed (unless the patient has previously had a positive treponemal antibody test). 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 or RPR is negative.

e. A point of care treponemal test (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. 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).

h. Anyone biologically capable of pregnancy who is diagnosed with syphilis should have a urine pregnancy test at their visit.

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 people living with HIV. 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, palms, or soles known as nickel and dime lesions (annular syphilis) 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. The only laboratory evidence of latent syphilis is a reactive VDRL or RPR with a positive TPPA or EIA (if at an outside laboratory). On occasion the nontreponemal test may be nonreactive.
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 or EIA (if at an outside laboratory). On occasion the nontreponemal test may be nonreactive.
    b. A lumbar puncture must 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). <u>Any neurologic symptom may be consistent with neurosyphilis.</u>

    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. Otosyphilis typically presents with tinnitus, vertigo, or sensorineural hearing loss which can be bilateral or unilateral. Otosyphilis should be treated as neurosyphilis, even if the LP results are normal.

    d. 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, including ocular syphilis or otosyphilis, the patient should be referred to ZSFG Emergency Department for

evaluation. If the patient has commercial insurance and a primary care provider, the patient can follow-up there or at an appropriate emergency department (e.g., UCSF, CPMC, St Francis' or St. Mary's Hospitals, or Kaiser) 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.

c. Evaluation of suspected ocular or otosyphilis must include a dilated eye exam by an ophthalmologist or audiometry by ENT, respectively. For isolated ocular or auditory findings, lumbar puncture (LP) may not be required during the evaluation as a normal CSF does not rule out ocular or otosyphilis; however, if there is evidence of other neurologic abnormalities, for example cranial nerve deficits, LP must be performed. 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 for suspected neurosyphilis, although CDC guidelines no longer require lumbar puncture for ocular or otosyphilis in the absence of other neurologic abnormalities on exam. 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/µl* or CSF protein > 40 mg/dl (this is considered "probable")

   c. Neurosyphilis is highly unlikely in the setting of a negative CSF FTA-ABS, especially with nonspecific neurologic symptoms.

**Note: In patients living with HIV, 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 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 (< 1 year duration) – Includes primary, secondary, and early latent syphilis
    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 people living with HIV.

       Pregnant patients 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 (> 1 year duration or of unknown duration)
    a. **Benzathine penicillin G** 2.4 million units IM every seven days for three doses, with no fewer than five days between doses. Pregnant patients (or those who can be become pregnant) should restart the three-dose series if more than nine days elapse between any doses. Non-pregnant patients who are receiving three doses of penicillin must restart their treatment if ≥ 14 days elapse since the last dose. If it has been 10-14 days since the last dose, consult with the attending to determine if the series must be restarted.
    b. For non-pregnant penicillin-allergic patients, **doxycycline** 100 mg orally twice daily for 28 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 they are 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 1-3 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 patients with a history of true penicillin allergy should be seen by the attending physician and referred for desensitization and treatment.*

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 people this reaction may be associated with early labor, so consider admitting for inpatient observation if in the second or third trimester. Any pregnant person 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 have a complete obstetric history documented at the initial visit to determine if there are other children who may have congenital syphilis. Pregnant people with syphilis should be linked to prenatal care. Serologic titers should be repeated no sooner than 8 weeks after treatment (if treatment occurs before 24 weeks gestation) and at delivery.

    c. If nontreponemal antibody titers have not declined fourfold by 12 months for secondary and early latent syphilis, or if they increased fourfold, the patient should be evaluated for re-infection or treatment failure and should be treated accordingly. Titers may decline more slowly in patients living with HIV, 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. At follow-up visits, if titers increase fourfold, or an initially high titer (> 1:32) fails to decline after 24 months, 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 have a complete obstetric history documented at the initial visit to determine if there are other children who may have congenital syphilis. Pregnant people with syphilis should be linked to prenatal care. Serologic titers should be repeated no sooner than 8 weeks after treatment (if treatment occurs before 24 weeks gestation) and at delivery.

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 ≥ 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 STIs 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 ≥ 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: (628) 217-6677.

Trichomoniasis

Trichomoniasis is a sexually transmitted infection caused by the single-celled protozoan parasite *Trichomonas vaginalis*. Patients with a vagina may be asymptomatic, or they may present with itching and malodorous vaginal discharge. Trichomonas infections in the penile urethra are usually asymptomatic, but urethritis may develop. Trichomoniasis is highly prevalent among cisgender women with HIV but is rare in cisgender men who have sex with cisgender men (MSM). There is a strong association with other STIs, particularly gonorrhea, so STI 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. Persons with a penis 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 or urine sample for trichomoniasis NAAT.
    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.
    e. Test for HIV, syphilis and other STIs as per clinic protocols.
4. Diagnostic Criteria
    a. Positive trichomoniasis NAAT by urine specimen or clinician-collected vaginal or endocervical swab ***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 (send trichomoniasis NAAT at time of treatment to confirm).

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

Single dose regimen of metronidazole 2 g has been shown to be less effective than a one-week course in cisgender women both with and without HIV, therefore the preferred first line regimen for trichomoniasis in all persons with a vagina is a 7 day course of metronidazole 500 mg twice daily. Metronidazole gel does not achieve therapeutic levels in the urethra and perivaginal glands and is not recommended.

Recommended initial regimens:

1. Vaginal infections:

   Metronidazole 500 mg twice daily for 7 days

2. Penile urethritis:

   Metronidazole 2 g orally once

3. Alternative initial regimen (all genders):

   Tinidazole 2 g orally once Persistent infection/treatment failure:

Rarely, resistance of trichomoniasis to metronidazole occurs. In evaluating patients for possible metronidazole-resistant trichomoniasis obtain a careful history to assess for re-infection and confirm that sex partner(s) were treated.

1. If re-infection is likely, re-treat with primary regimens above.

2. Patients with vaginitis 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

3. Cisgender males, and transgender females with a penis, who remain infected with T. vaginalis after a 2 g dose of metronidazole and have been re-exposed to an untreated partner should repeat the 2 g dose. If re-exposure is unlikely, they should be treated with metronidazole 500 mg orally twice daily for 7 days.

   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:

Metronidazole 500 mg orally twice daily x 7 days 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. Tinidazole should not be used in pregnancy as the safety is unknown.

Nitroimidazole allergy:

Patients with allergies to nitroimidazoles (metronidazole and tinidazole) should undergo oral de-sensitization.

C. Follow-up

1. Note that for 3 weeks after completion of therapy, nonculture tests (e.g., NAATs) may detect biologically inactive *Trichomoniasis* DNA and may yield false positive results.
2. All patients diagnosed with trichomoniasis should be re-tested in 3 months to rule-out re-infection.

D. Counseling/Education

Patients should:

1. Be counseled about the sexual transmission of trichomoniasis.
2. Understand how to take or use prescribed medications. CDC no longer recommends avoiding alcohol consumption while taking systemic metronidazole, as a review found no convincing evidence of a disulfiram-like interaction between alcohol and metronidazole.
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 trichomoniasis of the penile urethra frequently is asymptomatic.
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 (**metronidazole** 2 g orally once) should be offered 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 term "acute uncomplicated cystitis" refers to UTI with symptoms suggesting they are confined to the bladder. The most common uropathogen in uncomplicated UTIs is *Escherichia coli* (75-95%), followed by *Staphylococcus saprophyticus* and other species of Enterobacteriaceae, such as *Proteus mirabilis* and *Klebsiella pneumonae*. 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 (dysuria), frequency, urgency, suprapubic pain, and hematuria, but without fever or flank pain. Dysuria, frequency and urgency may occur from urethritis in the absence of bladder infection. Therefore, it is important to distinguish between urethritis (typically caused by gonorrhea, chlamydia or mycoplasma genitalium) and cystitis, particularly in a sexually active population. Those with sexually transmitted urethritis often have milder symptoms of longer duration, may have cervical infection, and often a history of a new sexual partner.

In young cisgender women, factors associated with increased risk of urinary tract infection include receptive vaginal intercourse, use of spermicide with or without diaphragm, history of a recent urinary tract infection and pregnancy. Cystitis is uncommon in adult cisgender men younger than 50 years of age but may be associated with insertive anal sex, being uncircumcised, and anatomic abnormalities in the genitourinary system. There is very little literature on the incidence, evaluation, or treatment of transgender women and men presenting with symptoms of a urinary tract infection, and evaluation and management should be based on the patient's symptoms, age, anatomy, and sexual practices.

Urinary tract infections can extend beyond the bladder to the kidney parenchyma (pyelonephritis) or the prostate (acute bacterial prostatitis) and can involve bacteremia. Signs of these complicated infections may include fever, chills, rigors, new fatigue or malaise, flank pain, costovertebral angle tenderness, pelvic pain, or perineal pain in persons with a prostate gland. Persons presenting with these symptoms should be referred to their primary care provider (if they have one), or to an urgent care center or emergency department for evaluation, including urine and blood cultures, as well as antibiotics. The following recommendations apply to the diagnosis and treatment of acute, uncomplicated cystitis at San Francisco City Clinic.

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 STI, and not necessarily a UTI, although UTIs can be associated with inadequate emptying of bladder and with intercourse ("honeymoon cystitis").

e. Cisgender men and transgender women should be asked about perineal pain and history of anatomic abnormalities of the genitourinary tract

2. Examination

a. In young non-pregnant cisgender 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 STIs, a pelvic exam should be performed to rule out vaginitis, cervicitis and PID.

3. Laboratory

a. Vaginal swab or urine for GC, CT, and M. gen NAAT.

b. For urinalysis to evaluate for UTI, 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.

e. The evaluation of uncomplicated cystitis in cisgender females does not require urine culture (unless recurrent, or persistent despite treatment)

f. If possible, people with a penis and suspected UTI should have a midstream urine culture collected. If not possible and the UTI is treated empirically, patients should be strongly advised to seek care if symptoms do not resolve despite treatment.

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 their PCP or urgent care for urine culture and sensitivity if they do not respond to therapy, or have pyelonephritis, suspected prostatitis, or recurrent infections.

B. Treatment

1. Uncomplicated cystitis

a. Cisgender women and transmen with a vagina

Recommended (non-pregnant):

1) **Nitrofurantoin** (Macrobid) 100 mg orally twice daily for 5 days OR

Alternate (non-pregnant):

1) Cephalosporins: **cefpodoxime** 100 mg orally twice daily for 5-7 days OR **cephalexin** 250-500 mg orally every 6 hours for 5-7 days
2) **Ciprofloxacin** 250 mg orally twice daily for 3 days
3) **TMP-SMX DS** One tab orally twice daily for 3 days

Recommended (pregnant):

1) **Nitrofurantoin** (Macrobid) 100 mg orally twice daily for 5-7 days OR
2) **Cefpodoxime** 100 mg orally twice daily for 5-7 days

b. Cisgender men and transgender women with a penis

Recommended:

1) **Nitrofurantoin** (Macrobid) 100 mg orally twice daily for 7 days

Alternative:

1) Cephalosporins: **Cefpodoxime** 100mg twice daily for 7 days *OR* **cephalexin** 250- 500mg orally every 6 hours for 7 days
2) Fluoroquinolones: **Ciprofloxacin** 500 mg orally twice daily for 5 days *OR*
3) **levofloxacin** 750 mg orally once daily for 5 days
4) **TMP-SMX DS** one tab orally twice daily for 7 days

c. Notes on treatment of UTI

1) Nitrofurantoin should not be used if early pyelonephritis is suspected due to poor concentration in the kidney.

2) Nitofurantoin and oral cephalosporins do not achieve reliable tissue concentrations in the prostate, thus if there is concern for early prostatitis, ciprofloxacin or levofloxacin should be used.

3) Fluoroquinolones such as ciprofloxacin should not be used in pregnancy

4) Moxifloxacin is NOT considered effective treatment in urinary tract infections.

5) Test of cure advised if cephalosporins used, though this is not available at SFCC.

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

7) As of August 2021, antibiotic susceptibilities of E. coli in urine isolates from UCSF were as follows: Nitrofurantoin 97%; cephalexin 90% when used for lower tract infections; ciprofloxacin 73%; TMP/SMX 69%; amoxicillin/clavulanate (Augmentin) 68% when used for lower tract infections.

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)

e. Symptoms greater than 7 days.

f. Pregnancy.

g. Diabetes.

h. Recent hospitalization or instrumentation.

i. Other significant underlying medical conditions.

<u>Treatment:</u>

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 STIs requires treatment of their sex partners as well. Current state law in California allows clinicians to provide additional courses of STI 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 STIs. 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 STIs. This concern has to be balanced against the need to quickly and efficiently treat exposed sex partners of MSM for bacterial STIs.

Patients diagnosed with the following STIs 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. **Trichomoniasis**

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 doxycycline or azithromycin if cotreating for chlamydia) 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 STI 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 STIs. 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. Non-rectal Lymphogranuloma venereum (LGV)
    l. Pelvic inflammatory disease (PID) not improved 72 hours after treatment
    m. Complicated urinary tract infection (UTI) or pyelonephritis
    n. Mycoplasma genitalium treatment failure
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 STI 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 STIs

Generic Name	Trade Name	Category in Pregnancy
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)
Famciclovir	Famvir	B
Fluconazole	Diflucan	C (avoid)
Imiquimod	Aldara	Avoid in pregnancy
Levofloxacin	Levaquin	C (avoid)
Metronidazole	Flagyl	Ok to use during pregnancy
Metronidazole gel	Metrogel	B
Miconazole	Monistat	B
Moxifloxacin	Avelox	C (avoid)
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 STI 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 For Providers

- California Prevention Training Center – STI Clinical Training
  (previously California STD/HIV Prevention Training Center)
  https://californiaptc.com/services/sti-clinical-training/

- CDC STI and Treatment Guidelines:
  http://www.cdc.gov/std/
  http://www.cdc.gov/std/treatment

- National STD Curriculum
  www.std.uw.edu

Appendix 1: Rectal symptoms protocol

Diagnostic Procedures for Rectal Symptoms