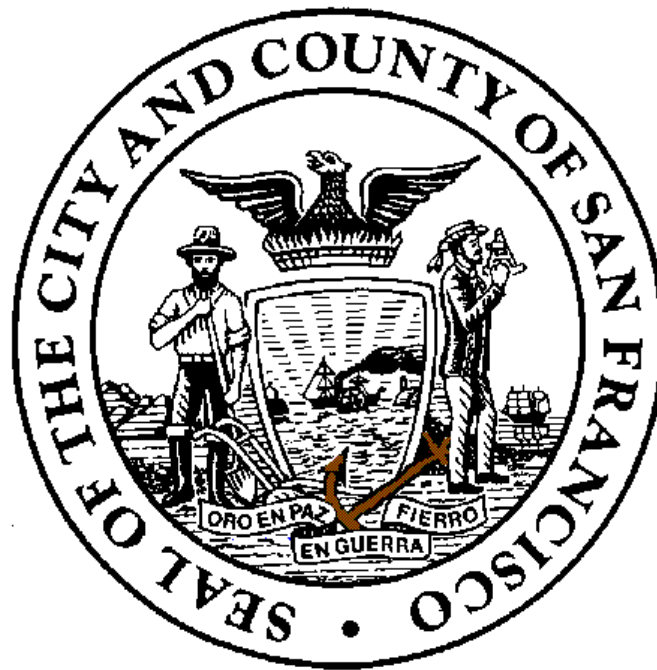


SAN FRANCISCO CITY CLINIC

CLINICAL PROTOCOLS

SEXUALLY TRANSMITTED DISEASES



Sexually Transmitted Diseases Prevention and Control Services
San Francisco Department of Public Health
San Francisco, California USA

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**SAN FRANCISCO CITY CLINIC
CLINICAL PROTOCOLS
SEXUALLY TRANSMITTED DISEASES**

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**Susan S. Philip, MD, MPH
Medical Director, San Francisco City Clinic**

**Jeffrey D. Klausner MD, MPH
Director, STD Prevention and Control Services**

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Actinomycosis in Women with IUD

Actinomyces israelii is a Gram-positive bacterium that may appear on the Pap smear or vaginal culture of an IUD user. While usually harmless, Actinomyces can cause a rare but serious form of PID in IUD users. When this happens, the condition is called “pelvic actinomycosis”.

Because pelvic actinomycosis is rare (whereas detection of actinomyces on Pap smear in IUD users is not), there is no clear-cut standard of care in asymptomatic women. Management decisions are further complicated by the fact that cytology labs frequently over-report the presence of actinomyces and the fact that the recommended treatment (Penicillin VK) has been poorly studied. Each case should be evaluated individually and may require consultation with the Attending Physician.

A. Diagnosis

History: Actinomyces noted on a Pap smear or culture result of IUD user.

B. Examination

Evaluate for signs of pelvic infection; lower abdominal tenderness, cervical motion tenderness, uterine/adnexal tenderness.

Laboratory: test for gonorrhea and chlamydia per San Francisco City Clinic screening recommendations for age and symptoms.

C. Treatment

1. For an asymptomatic patient:
 - a. Observe and repeat Pap smear in three months. If actinomyces is still present, document and repeat Pap smear every six months until Pap is negative.
 - b. Removal of an IUD is not necessary.
 - c. PCN VK treatment is not necessary.
2. If patient has symptoms of PID: refer to SFGH ER for further management after standard PID treatment started at San Francisco City Clinic.
3. If patient has cervicitis or asymptomatic gonorrhea or chlamydia infection, treat as in cervicitis, gonorrhea or chlamydia protocols.

Bacterial Vaginosis

Formerly called nonspecific vaginitis, Haemophilus vaginitis or Gardnerella vaginitis, bacterial vaginosis (BV) is the clinical result of alterations in the vaginal flora. *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. Recent 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 implicated in premature delivery and pelvic inflammatory disease, especially in women with an IUD in place, or who are undergoing instrumentation of the uterus (i.e. therapeutic abortion). Studies have also suggested that BV is associated with male-to-female HIV transmission may be due to an alkaline shift in vaginal pH and loss of H₂O₂ producing lactobacilli.

A. Diagnosis

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

B. Treatment: (Non-Pregnant Women)

1. The goal of treatment is to relieve signs and symptoms. Therefore, asymptomatic women should not be treated – the exception is in pregnant women with a history of premature labor (see below). In addition, because BV has been associated with PID following invasive procedures such as therapeutic abortion and endometrial biopsy, both asymptomatic and symptomatic women with BV should be treated before having such procedures performed.

Recommended regimens:

1. **Metronidazole** 500 mg PO BID for 7 days
2. **Metronidazole** gel, 0.75%, one full applicator intravaginally q HS for 5 days
3. **Clindamycin** cream, 2%, one full applicator intravaginally qhs for 7 days (patients should be told this is an oil based cream, and can weaken latex condoms)

Note: Clindamycin cream is less effective than Metronidazole po or gel.

Alternative regimens (lower efficacy for BV):

1. **Clindamycin** 300 mg PO BID for 7 days (note: keep in mind small risk of antibiotic-associated colitis)
2. **Clindamycin Ovules** 100g intravaginally once at bedtime for 3 days
3. **Metronidazole** 2 grams PO once (for patients unlikely to comply with longer regimen. Risk of relapse is higher with single dose therapy)

C. Treatment in Pregnancy

BV has been associated with preterm labor although the mechanism remains poorly understood.

1. High-risk pregnant women are those who have previously delivered premature infants. If BV is diagnosed, these women should be treated, regardless of symptoms.

Treatment:

1. **Metronidazole** 250 mg PO TID x 7 days or
2. **Metronidazole** 500mg PO BID x 7 days

Alternative Regimens:

1. **Clindamycin** 300 mg PO BID x 7 days

Note: Clindamycin cream has been associated with adverse events (prematurity and neonatal infections) in 3 trials so it is not recommended in pregnancy.

2. Low risk pregnant women (i.e., women who previously have not had a premature delivery) should treat for BV *only* if they are symptomatic.

Treatment: as above

D. Follow-Up

1. Routine follow-up is not recommended for non-pregnant women. Alternative treatment regimens may be used to treat recurrent disease (see below).
2. High-risk pregnant women should be advised to return in one month for repeat evaluation.

E. Counseling/Patient Education

Patients should:

1. Understand how to take or use prescribed medications and is instructed to avoid alcohol 24 hours before and after metronidazole administration.
2. Return for evaluation if symptoms persist or recur after treatment.
3. Refrain from douching.

Some experts recommend the following:

1. Advise patients use condoms, as this has been shown to be protective in some studies.
2. For women with recurrent BV a longer course of therapy (10-14 days) may be helpful. With persistent recurrence, consider prophylactic use of intravaginal metronidazole 1 applicator, qhs twice weekly for 3-6 months.

F. Evaluation of Sex Partners

Condoms may be helpful to reduce the frequency of recurrence. No clinical counterpart of BV is recognized in the male. The male partner can be offered a STD exam and appropriate screening and given relevant information on BV. Female partners of females diagnosed with BV have shown high rates of BV in several studies. Offer exam and evaluation.

Candida Balanitis

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

A. Diagnosis

1. History:
 - a. Rash on glans and/or prepuce.
 - b. Often pruritic.
 - c. Candidiasis in sexual partners.
 - d. Diabetes mellitus.
 - e. Immunosuppression, including HIV infection.
2. Examination:
 - a. Red rash with white flat lesions and possibly shallow ulcerations on glans, prepuce, and shaft.
 - b. Excoriations may be present.
3. Laboratory:
 - a. A KOH preparation of a skin scraping may reveal pseudohyphae or budding yeast.
 - b. If there is any question of diagnosis, a stat RPR and VDRL must be done to exclude syphilis.
 - c. Consider Herpes serology and/or PCR (or culture if PCR not available).
4. Diagnostic criteria:
 - a. History and clinical appearance consistent with above.
 - 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 BID x 7-14 days
2. **Miconazole** 2% cream BID x 7-14 days

3. **Tolnaftate** (tinactin) 1% cream BID 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 14 – 42 days in some cases. The area under the prepuce should be kept clean and dry.

Severe disease:

Fluconazole 150 mg po once, then repeated in three days (2 doses given to pt).

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

C. Follow-up

Routine follow up is not required.

D. Special considerations

Predisposing factors such as HIV infection and diabetes should be considered. Patients who may be at risk for HIV infection should be offered HIV antibody testing. Patients with symptoms of diabetes, a family history of diabetes or recurrent candida balanitis should have a urine dipstick test to screen for glucosuria. A primary care provider should evaluate patients if glucosuria is present.

Candidiasis in Women

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

A. Diagnosis

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

B. Treatment

Any of the following antifungal preparations are effective:

Vaginal:

1. **Clotrimazole** vaginal suppositories (100, 500mg) or cream (50mg per tube) x 1-14 days
2. **Miconazole** vaginal suppositories (100-200mg) or cream (2%, 4%) x 3-7 days
3. **Terconazole** vaginal suppositories (80mg) or cream (0.4%, 0.8%) x 3-7 days
4. **Butoconazole** 2% cream x 1-3 days

5. **Nystatin** suppositories x 14 days
6. **Tioconazole** 6.5% ointment 5 g intravaginally in a single application

Oral:

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

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

Note that single-dose therapy of vaginal creams have higher failure rates than three or seven day regimens. Clotrimazole and miconazole are available without prescriptions. Terconazole requires a prescription and is covered under Medi-Cal but is not available at SFGH. Vaginal creams and suppositories are considered safe in pregnancy and during lactation. Fluconazole (or other oral azoles) should not be used in pregnancy.

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

C. Follow-up

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

D. Counseling/Patient Education

Patients should:

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

E. Evaluation of Sex Partners

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

F. Recurrent Candidiasis

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

First try a longer duration of initial therapy before initiating a maintenance antifungal regimen (7-14 days of topical therapy or a repeat dose of fluconazole at day 3).

Recommended maintenance regimens (continue for 6 months, then trial period off therapy):

1. **Clotrimazole** 500 mg intravaginal suppository weekly
2. **Fluconazole** 100-150 mg PO weekly

One dose of fluconazole is less 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 and is often associated with severe burning and itching, but may have no positive microscopic findings. 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, nonindurated genital ulcerations with irregular, undermined borders. Unilateral or bilateral tender adenopathy occurs in approximately half the patients and an inguinal bubo (swollen 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. There is never a vesicular stage but chancroid may present initially as a small pustule that may be mistaken for folliculitis. It may also present as a raised, beefy red lesion. Complications of chancroid include phimosis or paraphimosis and ruptured buboes, which may result in fistulae. Also, studies from Africa, where chancroid is endemic suggest genital ulcer disease caused by *H. ducreyi* increases HIV transmission.

A. Diagnosis

1. History:
 - a. Male patients may present with a painful genital ulcer(s) and inguinal swelling or pain; female patients may present with a vulvar or vaginal ulcer(s) or with dysuria, bleeding, or vaginal discharge. Ulcer(s) in women may be relatively painless.
 - b. Obtain the following important historical characteristics:
 1. Duration of ulcer(s).
 2. Associated pain.
 3. Last sexual contact (may help to identify etiologic agent by an obvious incubation period). Note any travel history and sex contacts in areas outside of the Bay Area (South East U.S., Africa, Central or South America, Caribbean, and Asia).
 4. Use of systemic or topical antimicrobial agents.
 5. Use of other topical preparations (steroids, etc.).
 6. Signs or symptoms in partner(s).
 7. History of ulcers in the past and similarity of previous ulcers to current ulcer(s).
 8. As always, review the patient's history of previous STDs. If patient has a history of syphilis, obtain treatment history and note the date and titer of the last VDRL (or RPR). If the patient was treated for syphilis elsewhere, asks the patient if she/he knows the date of the last VDRL (or RPR) and whether or not it was still reactive.
9. HIV status.

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. Rectangular shaped ulcers are considered characteristic. The ulcers are usually sharply demarcated, but they may become confluent and quite large. They are generally not indurated, and are usually friable and deep. The base may be covered by a grey or yellow necrotic purulent exudate. Tenderness is usually, although not always, present. Painful and tender inguinal adenopathy is present in approximately 50% of patients.

A bubo is an enlarged inguinal lymph node that is tender and fluctuant. The skin overlying a bubo is often erythematous, quite thin and tense.

- c. Be sure to note the following characteristics:
 1. Number of ulcers.
 2. Location.
 3. Shape (oval, round, serpiginous, rectangular).
 4. Size.
 5. Nature of the ulcer(s) edges (raised, flat, undermined).
 6. Base of ulcer (purulent, clean).
 7. Depth of largest ulcer.
 8. Tenderness.
 9. Induration.
 10. Friability.
 11. Circumcision status of male.
 12. Inguinal adenopathy/bubo.

3. Laboratory:

Since ≥ 1 organism may coexist in a genital ulcer, all patients with a genital ulcer must have a darkfield examination, a stat RPR if the darkfield is negative (with follow-up VDRL), and a PCR assay or culture and serologic test for Herpes Simplex Virus infection.

4. Diagnostic criteria:

All suspected cases of chancroid should be presented to the Attending MD.

Clinical criteria, which will always be the necessary first step in diagnosis, will be based on the presence of painful ulcers on the genitalia (atypical ulcers may be painless), possibly accompanied by enlarged and tender inguinal nodes. Other causes of genital ulcers (i.e. herpes and syphilis) will be ruled in or out by

darkfield, RPR, and PCR assay or culture. Dual disease is possible and may not be ruled out on the day of presentation.

B. Treatment

Recommended regimens

1. **Ceftriaxone** 250 mg IM once, or
2. **Azithromycin** 1 gram PO stat

Alternative Regimens

1. **Ciprofloxacin** 500 mg PO BID for 3 days or
2. **Erythromycin** base 500 mg TID 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 20 gauge, 1-1/2 inch needle and syringe. First, cleanse skin with betadine. 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 seen 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 VDRL repeated one week and six weeks after therapy. HIV testing should be encouraged in any patient with negative or unknown HIV serostatus at the time of first visit and three months later. If there is no improvement at the 1-week follow-up, the Attending Physician should be informed.

D. Counseling/Education

Patients should:

1. Be referred to the Disease Control Investigator (DCI) for counseling and interview.
2. Understand how to take prescribed oral medications.
3. Avoid sex for at least 7 days and until the patient and partner(s) have completed therapy.
4. Use condoms to prevent future infections, and

5. Understand that chancroid has been associated with an increased risk of acquiring and transmitting HIV infection.

E. Evaluation of Sex Partners

All sex partners in the past 30 days of patients who have *H. ducreyi* infection should be examined and promptly treated with an appropriate regimen for *H. ducreyi* patient. Partners should be treated even with negative exams.

Chlamydia Trachomatis

Infection caused by *Chlamydia trachomatis* is one of the most common STDs in the United States. The single most important risk factor is young age. History of multiple partners, other STDs, and past infection with chlamydia are other risk factors. Infections in both women and men commonly occur without symptoms or signs. Women may complain of urinary frequency and dysuria; an increase in vaginal discharge; or lower abdominal pain. Men may have symptoms that include urethral itch, dysuria, and a mucoid-to-purulent discharge. Serious complications related to chlamydial infection include epididymitis in men; endometritis, salpingitis, infertility, ectopic pregnancy, chronic pelvic pain and postpartum infection in women; and conjunctivitis and pneumonia in infants. Chlamydia has a variable incubation period of approximately 7-21 days, but symptom onset may be delayed up to several months. Lymphogranuloma venereum (LGV), a rare disease caused by other serovars of *C. trachomatis* will be discussed in another section.

A. Diagnosis

1. History:

- a. Male patients may complain of dysuria and/or urethral discharge; typically the symptoms tend to be milder than for gonococcal urethritis and many men (>50%) may be asymptomatic. Rectal chlamydial infections may be asymptomatic, or may resemble gonococcal proctitis with pain, bleeding and mucous discharge.
- b. Female patients may have no symptoms. If symptomatic, women may complain of vaginal discharge, urinary frequency and dysuria, or lower abdominal pain.
- c. For symptoms of complicated infections in men and women, refer to the epididymitis and PID protocols.

2. Examination:

- a. Male patients with a urethral chlamydial infection may have a mucoid or purulent urethral discharge usually without inguinal adenopathy, although the exam may be normal.
- b. Male patients with rectal chlamydia may have signs of proctitis, although the exam may be normal.
- c. Female patients may have mucopurulent cervical discharge, cervical erythema, edema, and friability, although the exam may be normal.

3. Laboratory:

- a. At City Clinic all men and women under the age of 30 should be screened for chlamydia with a nucleic acid amplification test (NAAT) or by other available testing methods. Women who have undergone hysterectomy with complete cervical resection need not be screened.

- b. Diagnostic testing should be performed for all individuals with syndromes potentially caused by chlamydia; complaints or signs suggesting urethritis or epididymitis in men, cervicitis, PID, dysuria, pyuria and intermenstrual bleeding in women.

4. Diagnostic criteria:

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

B. Treatment of uncomplicated Chlamydia infections

Recommended Regimens:

1. **Doxycycline** 100 mg PO BID for seven days
2. **Azithromycin** 1-gram PO in a single dose orally for adolescents, those allergic to tetracyclines, or potentially nonadherent patients

Alternative Regimens:

1. **Ofloxacin** 300 mg orally BID for 7 days (more costly), or
2. **Levofloxacin** 500 mg orally po qd x 7 days (more costly)

Recommended Regimens for Pregnant Women – Doxycycline, ofloxacin and levofloxacin are contraindicated in pregnant women (clinical experience and preliminary data support that azithromycin is safe and effective in pregnancy):

1. **Azithromycin** 1 gram PO – single dose, or
2. **Amoxicillin** 500 mg orally TID for 7 days

Alternative Regimens:

Erythromycin (base or ethylsuccinate) are also recommended alternatives but these regimens may not be highly efficacious and have frequent side effects that often discourage patient adherence.

C. Follow-up

Taken as directed, the recommended antimicrobials are highly effective and post-treatment tests are not necessary for adherent patients. Note that for 3 weeks after completion of therapy, some nonculture tests (NAATs) may detect biologically inactive *C. trachomatis* DNA or antigen and may yield false-positive results. If a patient is being evaluated for re-infection and it has been less than 3 weeks since the initial treatment, testing with a nonculture method is not recommended. If there is strong suspicion of nonadherence or of re-infection, repeat empiric treatment should be given.

Test-of-cure at three weeks is only indicated in pregnant women, or for those treated with non-standard regimens.

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%).

Partner Treatment

All sex partners in the previous 60 days should be treated. Patients can be given treatment to give to partners with appropriate written instructions.

D. Counseling/Education

Patients should:

1. Understand the importance of regular screening (if MSM or <30 years old) since chlamydia is often asymptomatic.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination and treatment – Patients with chlamydial infection should be given medication to give to their partners.
5. Avoid sex for ≥ 7 days and until partner(s) have completed therapy.
6. Use condoms to prevent future infections, and
7. All patients with chlamydia should return in 3 months for repeat testing to rule out re-infection.

E. Evaluation of Sex Partners

All sex partners with the prior 60 days of patients who have *C. trachomatis* infection should be examined, tested, and promptly treated with an appropriate regimen. Patient or field delivered-therapy may be treatment options for patients or partners unlikely to come in for examination.

F. Special Considerations

All patients with chlamydial infection should have a gonorrhea test, either culture or NAAT; a VDRL, and be assessed for HIV testing.

Epididymitis

Epididymitis can be divided into a sexually transmitted form frequently associated with urethritis and commonly caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae* (usually occurring in men less than 35 years of age), and a nonsexually transmitted form associated with urinary tract infections and *E. coli* (usually occurring in men over 35 years of age). Symptoms and signs include pain in the scrotum, and tenderness, and swelling of the scrotal contents with or without urethral discharge. Epididymitis must be distinguished from testicular torsion. Torsion generally will occur in younger men, have a sudden onset, and present with the involved testicle lying higher in the scrotum than the uninvolved one and with the epididymis anterior instead of in its normal posterior position. Torsion is a surgical emergency so a prompt diagnosis is imperative in any man with scrotal pain and swelling.

A. Diagnosis

1. History:

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

2. Examination:

Patients with epididymitis will have scrotal swelling, tenderness, and possibly, scrotal redness; the epididymis itself 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. Note that epididymitis and testicular torsion can occur simultaneously. All cases of epididymitis should be presented to the Attending Physician.

3. Laboratory:

There are no characteristic laboratory findings unless urethritis is present. Urine-based gonorrhea chlamydia NAAT tests as well as all other appropriate STD screening must be done on all patients with epididymitis.

4. Diagnostic criteria:

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

B. Treatment

1. **Ceftriaxone** 250 mg IM once **and**

Doxycycline 100 mg PO BID for 10-14 days

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

2. Patients in whom a nonsexually transmitted etiology is suspected should be seen by the Attending Physician and treated with Ciprofloxacin 500 mg PO BID for 10-14 days. Ofloxacin 300 mg PO BID for 10 days is another alternative. Urologic consultation before treatment may be indicated. Optimally, men who have sex with men and heterosexual men > 35 should have a urine culture when available sent prior to treatment.

Indications for referral to ER:

1. Significant fever (>103.5);
2. Significant abdominal tenderness;
3. Toxic/acutely ill; extremely uncomfortable; or
4. Rule out torsion (especially in young men with abrupt onset).

C. Follow-up

Patients should be return for repeat evaluation in three days and demonstrate symptomatic improvement. Failure to improve within three days requires re-evaluation of the diagnosis or the therapy and consideration of urologic consultation. 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. Therefore, follow-up evaluation at one month to 6 weeks is indicated.

D. Counseling/Education

Patients with sexually transmitted acute epididymitis should:

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

E. Evaluation of Sex Partners

Sex partners of patients in past 60 days with sexually transmitted acute epididymitis should be evaluated for STDs and be promptly treated for gonococcal and chlamydial infections.

Genital Herpes

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. HSV infection is characterized by single or multiple vesicles anywhere on the genitalia, perineum or rectum. Vesicles rupture spontaneously to form shallow ulcers that may be very painful although not all individuals have painful lesions. Because the vesicular phase may be missed, especially in women, ulcers may be the first sign. Lesions heal spontaneously, without scarring. The first occurrence, called "first episode" or "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. The interval between clinical episodes is called "latency". Although viral shedding is greatest during symptomatic periods, viral shedding does occur intermittently during latency and accounts for asymptomatic transmission. Most anogenital herpes is caused by HSV-2; however increasingly, up to 50% of first episodes are caused by HSV-1. Anogenital HSV-1 infections are less likely to recur; therefore, PCR or cultures of recurrent lesions usually identify HSV-2 virus. On the basis of serologic studies, anogenital HSV-2 infection has been diagnosed in approximately 18% of the general sexually active population (45 million people) in the United States.

Herpes Zoster, which is a reactivation of Varicella Zoster (chickenpox) virus, is usually seen at City Clinic in HIV infected patients. Early in its course it may mimic HSV, but within hours or days it will become more widespread as it develops its dermatomal (or generalized) pattern. The Attending Physician should be consulted in possible cases of disseminated zoster.

A. Diagnosis

1. History:

- a. Patients may present with an initial episode of small blisters (vesicles) or with tender anogenital ulcers.
- b. Patients may present with a history of recurrent anogenital lesions that may or may not be painful.
- c. History of specific contact to an infected partner is infrequent and not necessary for diagnosis.

2. Examination:

- a. Intact vesicles may be present and are strongly suggestive of HSV infection.
- b. If ulcers and not vesicles are present then 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). When herpetic ulcers become confluent, they may present as a large, painful solitary ulcer that may be clinically indistinguishable from chancroid.

In addition, multiple shallow ulcers may appear in patients with primary syphilis particularly in those HIV infected.

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 should be sent, but additional evaluation of the ulcer is not necessary.
- b. For patients with a genital ulcer of unknown etiology, the full laboratory evaluation including HSV PCR or culture as outlined in the genital ulcer protocol must be done.
- c. Type-specific HSV-2 antibody serologic testing should be done at this visit to help identify the duration of HSV infection. HSV-2 PCR or culture positive, HSV-2 antibody negative patients have recent infection whereas HSV-2 culture positive, HSV-2 antibody positive patients may have long standing infection.

4. Diagnostic criteria:

- a. The appearance of vesicular lesions anywhere in the anogenital region. The cervix may be involved, particularly in primary outbreaks, and can be erythematous, with shallow ulcers that may appear necrotic and friable.
- b. Typical painful genital or anogenital lesion(s) and exclusion of other causes of genital ulcers are consistent with HSV infection.
- c. Recovery of HSV by PCR or tissue culture from vesicular fluid or scrapings of cervical, genital, or the anogenital lesions confirm the diagnosis.
- d. A positive type-specific antibody blood test signifies prior infection. However, PCR or HSV culture is necessary to confirm that the current symptoms are due to HSV.

B. Treatment for Primary or Initial Genital HSV Disease

Anti-herpetic agents may be used symptomatically to relieve and to shorten the duration of symptoms in patients.

Initial Episodes

1. **Acyclovir** 400 mg PO TID for 7 days, or
2. **Famciclovir** 250 mg PO TID for 7 days (more costly), or
3. **Valacyclovir** 1 g PO BID for 7 days (more costly)

Episodic Recurrent Infection

1. **Acyclovir** 400 mg PO TID for 3-5 days, or
2. **Acyclovir** 800 mg PO BID for 3-5 days, or
3. **Acyclovir** 800mg PO TID for 2 days, or

4. **Famciclovir** 125 mg PO BID for 5 days, or
5. **Valacyclovir** 500 mg PO BID for 3 days or Valacyclovir 1 gm daily for 5 days

C. Daily Suppressive Therapy

Suppressive therapy reduces the frequency of genital herpes recurrences by 70% - 80% among patients who have frequent recurrences (i.e. ≥ 6 recurrences per year), and many patients report no symptomatic outbreaks.

Also patients who report marked anxiety/depression due to recurrent herpes may benefit from daily suppressive therapy. Suppressive therapy may also reduce the transmission of HSV infection from infected to uninfected partners.

Asymptomatic viral shedding is more frequent in genital HSV-2 infection than genital HSV-1 infection and is most frequent in the first 12 months of acquiring HSV-2. Typical suppressive regimens are as follows:

1. **Acyclovir** 400 mg orally BID, or
2. **Famciclovir** 250 mg orally BID, or
3. **Valacyclovir** 500 mg orally once a day, or
4. **Valacyclovir** 1 gm orally once a day

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

D. Pregnancy

Acyclovir use during pregnancy is generally safe; the same probably holds for lactating women. First episode of genital herpes in pregnant women may be treated with oral acyclovir. Patients with recurrent genital herpes should be referred to their prenatal provider for management.

E. 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 must return in one week for a repeat evaluation including a repeat VDRL (see genital ulcer protocol).

F. Counseling/Education

Patients should:

1. Understand how to take prescribed oral medications.
2. Keep the lesions clean and dry.
3. Return for evaluation if symptoms persist or recur after treatment.
5. Be counseled about HSV transmission.
6. Avoid sex while lesions are present.
7. Understand that a lesser, but real, risk of transmission exists during asymptomatic periods.

8. Use condoms to help decrease transmission.
9. Inform prospective sex partners of risk of exposure.
10. Refer sex partner(s) with lesions for evaluation.
11. For women: if pregnant, tell clinician/obstetrician about the history of herpes.
12. Understand that genital herpes (and other genital ulcer diseases) has been associated with an increased risk of HIV transmission.

G. Evaluation of Sex Partners

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

H. Special Considerations

Infection during pregnancy:

A majority of women with a history of genital herpes can deliver their infants vaginally. Women with recurrent infection are at much lower risk for transmission of the virus to the neonate during vaginal delivery than women with primary infection during delivery. Acquiring the initial infection during late pregnancy increases the likelihood of maternal-to-infant transmission. Weekly cultures near the time of delivery are not recommended because they do not predict the shedding of HSV at the time of delivery. The risk of perinatal transmission during a vaginal delivery in a woman with primary infection (culture positive, HSV-2 antibody negative) is approximately 20-50%, whereas the risk is <1% in women with vulvar recurrences (prior infection, HSV-2-antibody positive). Because this risk is so great and because neonatal HSV infection is quite serious, most experts recommend that women with primary HSV infections at the time of delivery should be delivered abdominally. Pregnant patients in whom an HSV infection is diagnosed should inform their obstetrician. Pregnant women should be counseled that primary HSV-I infection could occur through oral sex with a partner with orolabial herpes (cold sore).

Genital Ulcer Disease

Genital 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 genital ulcers include lymphogranuloma venereum (*Chlamydia trachomatis*, serovars L1, L2, L3) discussed in a separate section, and granuloma inguinale (*Calymmatobacterium granulomatis*); which is rare in the United States and will not be addressed here. This protocol outlines the general evaluation of a patient with a genital ulcer. For specifics regarding the management of a patient with a genital ulcer for which the diagnosis has been established, please refer to the protocol regarding the specific disease entity. The etiologic diagnosis of a genital ulcer by clinical presentation alone, even by experienced clinicians, is unreliable. Therefore, a thorough clinical and laboratory evaluation of all genital 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 should still be drawn, but further work up for diagnosis is unnecessary.

A. Diagnosis

1. History:

- a. Duration of ulcer.
- b. Painful vs. painless.
- c. Was lesion a fluid-filled blister (vesicle) (e.g., HSV).
- d. Last sexual contact (may help to identify etiologic agent by an obvious incubation period).
- e. Use of systemic or topical antimicrobial agents.
- f. Use of other topical preparations.
- g. Symptoms or signs in partner(s).
- h. History of ulcers in the past and similarity of previous ulcers to current ulcer(s); do they occur in same location (e.g., HSV).
- i. Symptoms such as tingling/itching prior to appearance (e.g., HSV).
- j. Sexual contact outside San Francisco Bay Area, including recent travel.
- k. As always, review the patient's history of previous STDs. If patient has a history of syphilis, note the date and titer of the last VDRL. If the patient was treated for syphilis elsewhere, ask the patient if s/he knows the date of the last VDRL and if it was reactive. Always attempt to obtain an accurate treatment history.

2. Examination: Describe the following characteristics of the genital ulcer(s) and lymph nodes.
 - a. Ulcer(s):
 1. Number
 2. Location
 3. Shape: oval, round, serpiginous, rectangular
 4. Size of largest ulcer in centimeters
 5. Nature of the edges: raised, rolled, flat, undermined
 6. Base of ulcer: purulent, clean
 7. Approximate depth of largest ulcer
 8. Tenderness
 9. Induration
 10. Friability
 - b. Lymph node(s):
 1. Number and location of enlarged nodes
 2. Size
 3. Tenderness
 4. Presence of bubo (if bubo present, check for fluctuance-the Attending Physician should see any patients with a fluctuant bubo and drain it)
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. Discuss with Attending Physician culture for *H. ducreyi*.
 - d. Stat RPR, VDRL and clinician-ordered TPPA (per lab protocol, the TPPA is not run if the VDRL is negative as is often seen early in primary syphilis. The TPPA may be positive before the VDRL, so it is important to ask the lab to run the TPPA regardless of the VDRL result in suspected early cases).
 - e. HSV-2 type specific serology.
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, make a presumptive diagnosis of primary syphilis (refer to syphilis protocol).
 - c. If the stat RPR is negative, make a presumptive diagnosis of either HSV or chancroid 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 there remains great uncertainty, 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.
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 recent episode.

C. Follow-up

1. If herpes diagnosis is certain, no follow-up is necessary (refer to HSV protocol). Other patients with nonvesicular genital ulcers 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 VDRL. 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. In the case of an ulcer that was diagnosed as chancroid, and the initial VDRL was negative, repeat the VDRL and TP-PA in six weeks.

D. Counseling/Education

1. Explain to the patient how to take the prescribed medication.
2. Explain the follow-up schedule.
3. Discuss with patient the need to evaluate partner(s) (past 90 days); the DCI (Disease Control Investigator) will cover this in more detail.
4. Advise avoiding sex for at least 7 days until patient and partner(s) have been fully treated.
5. Make certain that patient understands HIV infection is associated with to genital ulcer disease.
6. Offered HIV testing and repeat testing at 3 months.
7. Use condoms to prevent future infections.

E. Evaluation 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. The DCI can make a better judgment on the disposition of partners when all the tests are completed.

F. Reporting

Report suspected syphilis cases to STD Control within 24 hours.

Genital Warts

Genital warts, or *condyloma acuminata*, are caused by many subtypes of human papillomavirus (HPV), small DNA viruses. HPV is the most common sexually transmitted infection in the US. It 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 can be painless, 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. Exophytic (fleshy) warts are usually caused by HPV types 6 or 11; flat warts are caused by “higher” types (e.g., HPV types 16, 18, 33 and 35) and are more often associated with vaginal, anal and cervical dysplasia. There is no way to clinically differentiate the various types. However, regardless of HPV type, the majority of infections are subclinical (no visible warts). Subclinical infection of the cervix is best assessed by regular Pap smears, followed by colposcopy and biopsy if necessary. Biopsy is also necessary for pigmented or atypical external warts to rule out malignancy.

A. Diagnosis

1. History:

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

2. Examination:

- a. Typical 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 genital warts.

- b. All patients with an initial diagnosis of genital warts must have a VDRL done, and other STD screening if indicated.
4. Diagnostic criteria:
- a. Appearance of typical condyloma. Any atypical or deeply pigmented lesions on the genitals, perianal area, or rectum should be referred for biopsy. Possible *Condyloma lata* must be evaluated by darkfield microscopy and rapid RPR.
 - b. Demonstration of atypical cytologic changes on Pap smear of cervical cells (only suggestive of HPV infection).

Note: Tests for the detection of cervical HPV-DNA are available, but these tests are not used for clinical management of individual patients with abnormal Pap smears at City Clinic.

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 genital warts, there are no clear medical indications supporting routine therapy. There is no evidence that wart treatment prevents transmission or the development of genital HPV-related cancers.

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

Provider-Administered Therapies:

1. **Liquid nitrogen (LN2)** can be applied topically with a swab. The swab should be left on the wart(s) for a slow 10 count, the wart should be allowed to thaw, and then the treatment should be repeated. The freeze/thaw cycle results in cell cytolysis - destroying the wart. Side effects include discomfort up to 15 minutes after the procedure, erythema and possible blistering at treatment site. Multiple treatments at three-week intervals are usually required.
2. **Podophyllin, 25%** can be applied topically with a swab. It is a plant extract that inhibits cell division. The podophyllin must dry completely so that normal skin does not come into contact with the medication, and patients must be instructed to wash the podophyllin off 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. Podophyllin has the potential to be neurotoxic, oncogenic, teratogenic and mutagenic and so should not be used in pregnancy or to treat extensive warts with a large surface area. Side

effects may include erythema, ulceration or pain at treatment site within 48 hours after application.

3. **Trichloroacetic acid (TCA)** in alcohol is useful for warts on mucous membranes. It can be applied with the end of a cotton swab. Extreme care must be used when applying it to prevent burns. Avoid all contact with normal skin around wart. TCA causes a chemical coagulation of cell proteins, which destroys the wart. Side effects include pain, erythema, burning, and ulceration.
4. **Electrocautery, surgical excision.** For severe disease – requires referral to appropriate specialist.

Patient Applied Therapies:

1. **Podofilox 0.5%** solution (3.5 ml) or gel (3.5g) is applied with a cotton swab or finger (with gel) to visible warts BID for three consecutive days followed by four days without treatment. This cycle can be repeated as necessary for a total of four times. 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 (\$102/3.5ml solution at Walgreens) and is covered by Family PACT. Should not be used in pregnancy.
2. **Imiquimod 5%** cream (distributed in small packets) to be applied with fingertip at bedtime three times a week for as long as sixteen 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 and ulceration. Imiquimod is available only by prescription (\$182/one month treatment at Walgreens) and is covered by Family PACT. Should not be used in pregnancy.

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 Proctology Clinic, San Francisco General Hospital (SFGH). The Proctology Clinic performs a more comprehensive proctoscopic exam and will biopsy internal warts if found. Appropriate treatments are offered.

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, SFGH 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 genital warts and HPV.
2. Return for provider-applied treatment every three weeks until lesions have disappeared.
3. Understand that after treatment of visible warts, the potential for transmission may persist and that recurrences are very common.
4. Know 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.

Consistent condom use has been shown to decrease the acquisition of HPV and incidence of external genital warts in men and reduce HPV acquisition in women.

5. Continue regular Pap smears (whether warts are present or not) which are the best screening tools for the cervical dysplasia that can be associated with HPV.

E. Evaluation of Sex Partners

Current sex partners of patients with HPV infection can be examined for 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 examined for other STDs and female partners should be up to date on their Pap smear.

F. Special Considerations

Genital warts in pregnancy:

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

G. 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 visible cervical warts and squamous intraepithelial lesions (SIL) on Pap smear should be referred for colposcopic evaluation. Consult the Pap smear protocol for further details.

Gonorrhea

Sexually transmitted infections caused by the gram-negative bacterium *Neisseria gonorrhoeae* (GC) may be symptomatic or asymptomatic. GC can infect the urethra, cervix, rectum, pharynx, and in rare cases may become disseminated (bloodborne). It has a short incubation period of 1-10 days (average 2-5 days). Infections caused by antimicrobial-resistant *N. gonorrhoeae* are clinically indistinguishable from those caused by antimicrobial-susceptible strains. Symptomatic men usually have purulent urethral discharge often accompanied by pain with urination. Women may have abnormal vaginal discharge, abnormal bleeding, pelvic pain, or pain with urination. Although the data on asymptomatic infection are limited, as many as 50-70% of women may be asymptomatic. Additionally, in men who have sex with men (MSM) the majority of gonococcal infections in the rectum and pharynx are asymptomatic. Serious complications of gonococcal infection include pelvic inflammatory disease with subsequent infertility or risk of ectopic pregnancy in women, and epididymitis and urethral stricture in men. Disseminated gonococcal infection (DGI) may occur in either sex, but is not common. Untreated infection in pregnancy may result in premature delivery, including stillbirth. Newborns of women with untreated infection are at risk for gonococcal eye infection (*ophthalmia neonatorum*), scalp abscess at the site of fetal monitors, and disseminated infections.

A. Diagnosis

1. History: Symptoms will vary depending on the site of infection. Women should be evaluated for PID if they present with appropriate symptoms (see PID protocol for details).
 - a. Cervix - patients may present with vaginal discharge, lower abdominal pain, pain with intercourse, post coital bleeding, and pain with urination.
 - b. Urethra – pain with urination, discharge.
 - c. Rectum - discharge (usually described as mucous on stools), tenesmus, perianal itching, rectal pain and possibly rectal bleeding.
 - d. Pharynx – Usually asymptomatic, or patients may complain of a sore throat or pain with swallowing.
 - e. DGI – see section H 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 must use anoscope for proper rectal examination).
 - d. Pharynx – rarely redness, exudate (most have no signs of infection and when present are nonspecific).

e. DGI – see section H below.

3. Laboratory:

- a. A Gram stain of the discharge should be done.
- b. Screening of all exposed sites should be done. Pharyngeal screening is done for men who have had oral receptive sex with multiple partners. Rectal screening should be done on all patients who report any receptive anal sex in the previous six months, regardless of condom usage. Patients may be treated based upon possible exposure.
- c. A VDRL should be done on all patients evaluated for GC.

4. Diagnostic Criteria:

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

B. Treatment of uncomplicated infection (pharynx, cervix, urethra and rectum)

California is a state with increased prevalence of fluoroquinolone-resistant gonorrhea; therefore, these drugs should not be used to treat GC.

Treatment for GC requires simultaneous treatment for chlamydia, unless chlamydia has been ruled out by laboratory testing, as co-infection occurs in 20-30% of cases.

Recommended Regimens:

1. **Cefpodoxime** 400mg (Vantin) orally once and **doxycycline** 100 mg orally BID for 7 days as co-treatment for chlamydia (or azithromycin 1 gm orally once), or
2. **Ceftriaxone** 125 mg IM in a single dose with chlamydia co-treatment as above.

Alternative Regimens:

Note: for individuals with penicillin allergy (defined as hives, angioedema or anaphylaxis):

1. **Spectinomycin** 2 gm IM once with chlamydia co-treatment as above (not readily available), or
2. **Azithromycin** 2 grams orally once, for those allergic to tetracyclines, or for potentially non-adherent patients (warn patients about increased G.I. side effects).

Note: Spectinomycin may not be effective against pharyngeal gonorrhea. The safety of spectinomycin in pregnancy has not been established, but there have been no reported cases of maternal or fetal toxicity. Azithromycin is the drug of choice for co-treatment of Chlamydia for pregnant women. Doxycycline cannot be used in pregnant or lactating women.

C. Treatment of DGI – see section H below and call for expert consultation: 487-5595

D. Follow-up

Symptoms that persist after treatment are likely due to reinfection rather than treatment failure. Patients should be questioned regarding the possibility of reinfection, 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* and write "Rx failure" on the lab slip.

1. Test-of-cure 3 weeks after treatment is only indicated for pregnant women.
2. All patients should return for repeat testing for GC **three months** after treatment.

E. Evaluation 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 promptly treated for *N. gonorrhoeae* and *C. trachomatis*.

Patient-delivered partner therapy (PDPT) should be offered to all patients with GC. Men should be strongly encouraged to also refer female partners to the clinic or MD for evaluation.

F. Counseling/Education

Patients should:

1. Be counseled to notify sex partners and offered patient-delivered partner therapy.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Avoid sex for 7 days.
5. Use condoms to prevent future infections.
6. Advised to return at 3 months for repeat testing to rule out re-infection.

G. Special Considerations

All patients with gonococcal infection must have a VDRL done. Patients who were called back to the clinic because a screening test was positive do not need a repeat VDRL if the initial VDRL was done in the previous week was non reactive.

H. Disseminated Gonococcal Infections (DGI)

Although the incidence of DGI has declined, it is important to note *N. gonorrhoeae* can cause bacteremia and systemic infection including arthritis, meningitis,

endocarditis, tenosynovitis and diffuse skin eruption characterized by small pustules. Patients with suspected DGI should be evaluated by the Attending Physician. DGI should be considered if a patient has signs of fever, pustular skin lesions, stiff neck, headache, acute swelling, pain, erythema of a joint (often a single joint) and/or tenosynovitis - redness, swollen or tender tendon sheath(s).

Recommended therapy for DGI includes 7 days of high dose anti-gonococcal antibiotics such as:

1. **Ceftriaxone** 1 gm IM or IV every day for 7 days
2. **Cefpodoxime** 400mg po BID for 7 days

Consider hospitalization for severe disease. Otherwise patients can be treated as outpatients initially with IM or IV Ceftriaxone with daily clinical evaluation until they demonstrate improvement and then complete the remainder of the seven-day course with oral medication.

Hepatitis A and B

Vaccine Preventable STDs

One of the most effective methods to prevent the acquisition of STDs is pre-exposure immunization. Currently licensed vaccines for the prevention of STDs include those for hepatitis A and hepatitis B. City Clinic is currently offering the hepatitis A and B vaccine series to eligible patients.

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 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: 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 0.3%, but is higher (1.8%) in adults over 49 years and one study suggested among those with chronic hepatitis C mortality may be as high as 40%. HAV infection is not associated with chronic liver disease.

Outbreaks of hepatitis A among men who have sex with men have been reported in urban areas, both in the U.S. and abroad. The prevalence of HAV infection among men who have sex with men has been found to be significantly higher than that among heterosexual men (30% vs. 12%) in one study. A case-control study of men who have sex with men with acute hepatitis A conducted in New York City found cases to have more anonymous sex partners and to be more likely to have engaged in group sex than controls; oral-anal intercourse (oral role) and digital-rectal intercourse (digital role) were associated with infection.

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, and
2. Persons who have used injection drugs in the past year.

Dosing

Adults - **Havrix** (1440 EL.U) or **Vaqtia** (50 units) Hepatitis A vaccine IM at 0 and 6 months. No need to repeat or restart if doses are late.

Postexposure Prophylaxis

Non-immune patients exposed to a person with acute HAV (household, sexual or IDU contact) should receive HAV immune globulin. This is available through Tom Waddell Clinic or the Adult Immunization Clinic. They should also begin the HAV vaccination series (at a separate injection site) as outlined above.

Hepatitis B

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

Pre-exposure Prophylaxis

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

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 without testing. 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.

Dosing

Adults/Adolescents - **Recombivax**(5mcg) or **Engerix** (10mcg) Hepatitis B (IM) at 0,1, and 4 months. No need to restart or repeat doses if missed or late.

Persons > 20% ideal body weight ,smokers or HIV positive with CD4<300 need **Recombivax** (10mcg) or **Engerix** (20mcg) Hepatitis B IM at 0,1,4 months.

Post Exposure Prophylaxis

Exposure to Persons with Acute Hepatitis B

Sexual contacts: Persons with acute HBV infection are potentially infectious to sexual contacts. Passive immunization with hepatitis B immune globulin (HBIG) has been shown to prevent 75% of these infections. Sexual contacts of persons with acute hepatitis B should receive HBIG if available and begin the hepatitis B vaccine series immediately. Testing of sexual partners for susceptibility to HBV infection (anti-HBc or anti-HBs) can be considered if it does not delay treatment beyond 14 days.

Non-immune persons recently exposed to hepatitis B can receive HBIG at Tom Waddell Clinic, if available.

Exposure to Persons with Chronic HBV Infection

Sexual and nonsexual household contacts: Hepatitis B vaccination without the use of HBIG is highly effective in preventing HBV infection in household and sexual contacts of persons with chronic HBV infection. All such contacts should be vaccinated.

Special Considerations

Pregnancy:

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

Lymphogranuloma Venereum

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

A. Clinical Presentation:

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

The proctitis syndrome, more commonly seen in MSM in recent outbreaks, is characterized by rectal discharge, bleeding, and painful inflammation progressing to proctocolitis. Rare complications of LGV include chronic inflammation with development of genital elephantiasis, fistulas, and rectal strictures, sometimes requiring surgical intervention.

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

B. Diagnosis:

Currently, there is no standardized diagnostic test for the diagnosis of LGV. Therefore consider the diagnosis based on a compatible clinical presentation. In MSM with bloody proctitis or tender inguinal lymphadenopathy, providers should collect specimens to test for chlamydia (NAAT and culture) and presumptive treatment should be initiated. Nucleic Acid-Amplification Tests (NAATs) are very sensitive for chlamydia but do not further identify the LGV serovars. The chlamydia culture, though not as sensitive as the NAAT, may be DNA sequenced to identify LGV serovars; however, chlamydia cultures are not widely available. LGV serology is not helpful for diagnosis.

C. Treatment:

1. **Doxycycline** 100 mg PO BID for 21 days

Alternate:

1. **Azithromycin** 1 gram PO qweek x 3 weeks may be effective, but clinical data are limited
2. **Erythromycin** 500 mg PO QID for 21 days

D. Follow-up:

Patients should return to clinic if symptoms persist past treatment. All patients with a positive chlamydia test should return to clinic in 3 months for repeat testing.

Patients should also be tested for gonorrhea, syphilis (VDRL or RPR) and other STDs as necessary.

E. Partners

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

Treatment should be given as partner delivered therapy.

1. Doxycycline 100mg bid x 7 days or
2. Azithromycin 1g po once

Partners should also be told that if they develop symptoms of proctitis (rectal discharge, irritation) or inguinal lymphadenopathy they should present for a full clinical evaluation.

F. Counseling/Education

Patients should:

1. Understand that LGV is currently treated presumptively as a clinical syndrome in MSM.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination and treatment. Patients should be given medication to give to their partners – note that partners should be given standard therapy for Chlamydia (see section E above).
5. Avoid sex until both they and their partner(s) are fully treated.
6. Use condoms to prevent future infections.
7. All patients should return in 3 months for repeat testing for chlamydia.

Molluscum Contagiosum

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

A. Diagnosis

1. History:

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

2. Examination:

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

b. The remainder of the exam is usually normal.

3. Laboratory:

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

4. Diagnostic criteria:

a. Typical papules.

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

B. Treatment

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

C. Follow-up

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

Patients should also be screened for other STDs, based on their risk factors.

D. Counseling/Education

Patients should:

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

E. Special Considerations

Extensive molluscum, repeated recurrence after treatment or appearance of lesions on the face are common in patients with cellular immunodeficiency and should raise the suspicion of HIV infection. Treatment for HIV-infection with highly active antiretroviral therapy (HAART) has been shown to reduce the occurrence of molluscum in HIV-infected patients.

Mucopurulent Cervicitis

Mucopurulent cervicitis (MPC) is a clinical syndrome characterized by a mucopurulent cervical exudate and endocervical friability. Patients may be asymptomatic. *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* are among the pathogens associated with MPC, but in most cases no etiologic organism can be identified. Herpes simplex virus and *Trichomonas vaginalis* can also produce cervicitis but these infections tend to affect 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.

A. Diagnosis

1. History:
 - a. MPC is frequently asymptomatic.
 - b. If symptomatic, patient may complain of vaginal discharge, coital bleeding, pain with intercourse, pain with urination, or intermenses bleeding.
 - c. The patient may have a partner who was diagnosed with urethritis.
2. Examination:
 - a. Mucopurulent cervical discharge. A positive swab test is defined by the finding of exudate (yellow discoloration) on the first swab after insertion into endocervix. It is often helpful to hold the swab against a white paper background for contrast.
 - b. Cervical erythema, edema, and/or friability (bleeding) are often present after the first swab is inserted.
3. Laboratory:
 - a. A Gram stain of the cervical discharge may reveal white blood cells and gram-negative intracellular diplococci.
 - b. Send a vaginal swab for gonorrhea and chlamydia Nucleic acid amplification (NAAT) testing.
 - c. All patients should have a VDRL.
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. Degree of cervical ectopy should be charted and noted (1-3°) as inflammation in the zone of ectopy can produce yellow swab from endocervix without accompanying infection.

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

B. Treatment

The results of the chlamydia and gonorrhea test should determine the need for treatment, unless the likelihood of infection with either organism is high based on recent exposure or prior infection. Adolescents, patients unlikely to return for treatment, and symptomatic women, should be treated empirically for chlamydia. Anti-chlamydial treatment will treat both chlamydia and mycoplasma genitalium infections which account for at least 20% of cases.

If gonorrhea is identified on Gram stain, or the patient is in a high risk group for gonorrhea (age <25, previous GC, African-American):

1. **Cefpodoxime** 400mg PO x 1 AND treatment for Chlamydia as below:

If a cervical gram stain is negative for GC:

1. **Doxycycline** 100 mg PO BID for seven days
2. **Azithromycin** 1 gm PO once

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

C. Follow-up

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

D. Counseling/Education

Patients should:

1. Be counseled about the potential health consequences of untreated MPC.
2. If indicated, understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist.
4. Based on test results, refer sex partner(s) for examination and treatment.
5. If treated, abstain from sex for at least 7 days and until sex partners have been treated.
6. Use condoms to prevent future infections.

E. Evaluation of Sex Partners

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

Patient-delivered partner therapy should be given for partners unlikely to come in for evaluation and treatment, especially if chlamydia is strongly suspected as the cause of MPC.

Nongonococcal Urethritis

Nongonococcal urethritis (NGU) is characterized by a mucoid or mildly purulent urethral discharge often accompanied by discomfort or burning with urination or urethral itching. The incubation period of NGU may be one to five weeks, so is considerably longer than for gonorrhea. However, it is not possible to differentiate gonorrhea from NGU based on clinical presentation alone. On microscopy, the diagnosis can be made if white blood cells are present and Gram-negative intracellular organisms are absent. *C. trachomatis* is the most frequent cause of NGU (i.e., in 20% of cases); however, the prevalence differs by age group, with lower prevalence among older men; the overall proportion of NGU cases caused by chlamydia has been declining. Complications of NGU among men infected with *C. trachomatis* include epididymitis and Reiter's syndrome. *Mycoplasma genitalium* is another cause of NGU. While FDA approved diagnostic tests for *Mycoplasma genitalium* are not yet available, current standard treatments for NGU are effective against both Chlamydia and Mycoplasma. *Trichomonas vaginalis* and HSV cause NGU less commonly. Diagnostic and treatment procedures for these organisms are reserved for situations in which NGU is unresponsive to therapy.

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

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 present with pain or burning with urination 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 quite purulent and indistinguishable from gonorrhea on clinical grounds.
 - c. Patients may also present with minimal symptoms of itching/irritation at the urethral meatus.
2. Examination:
 - a. Examine the urethra for discharge.
 - b. If discharge is not present, "milk" the penis to see if an exudate can be expressed.

3. Laboratory:

- a. If a discharge is present, a Gram stain should be done to look for white blood cells and gram-negative diplococci.
- b. Culture or nucleic acid amplification test (NAAT) for gonorrhea.
- c. Urine NAAT for Chlamydia.
- 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 2000 rpm x 5 minutes).

4. Diagnostic criteria:

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

- a. Mucopurulent or purulent discharge.
- b. Gram stain of urethral secretions demonstrating ≥ 5 WBCs per high power field (100x). The Gram stain is the preferred rapid diagnostic test for evaluating urethritis. It is 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.
- d. ≥ 10 WBC per high power field (40x) on spun urine sediment.

If none of these criteria are present, treatment should be deferred, and the patient should be tested for *N. gonorrhoeae* and *C. trachomatis* and followed closely. If the results demonstrate infection with *N. gonorrhoeae* or *C. trachomatis*, the appropriate treatment should be given and sex partners referred for evaluation and given patient delivered partner therapy (PDPT).

Empiric treatment of symptoms without documentation of urethritis is recommended only for patients at high risk for infection who are unlikely to return for a follow-up evaluation (e.g., adolescents and men who have sex with men who have multiple partners). Such patients should be treated for chlamydia/NGU. Partners of patients treated empirically should be referred for evaluation and treatment and given PDPT.

5. Further Testing

- a. In patients reporting significant urethral discomfort without discharge, consider performing a swab of the meatus for HSV PCR.
- b. Patient should have a VDRL drawn, and urine sent for gonorrhea and chlamydia as well as other indicated STD testing.

B. Treatment

Treatment should be initiated as soon as possible after diagnosis. Single dose regimens offer the advantage of directly observed therapy and should be used if the

risk of non-adherence is high. If multiple-dose regimens are used, the full course of medication should be provided in the clinic or health-care provider's office.

Recommended Regimens:

1. **Doxycycline** 100 mg orally BID for 7 days*, or
2. **Azithromycin** 1 g orally in a single dose (more costly)

**Doxycycline is treatment of choice for NGU in MSM due to its potential benefit in incubating syphilis*

Alternative Regimens:

1. **Ofloxacin** 300 mg BID for 7 days, or
2. **Levofloxacin** 500 mg daily for 7 days

C. Counseling/Education

Patients should:

1. Be counseled about urethritis.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination and be given treatment for partners.
5. Avoid sex for at least 7 days and until partner(s) are treated (include the period when both partners are taking medication).
6. Understand that oral flora may cause urethritis, so they may develop NGU after oral sex with a monogamous partner.
7. Use condoms to prevent future infections

D. Follow-Up for Patients Who Have Urethritis

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. Patients should be instructed to abstain from sexual intercourse for at least 7 days after initiation of therapy.

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

E. Partner Referral

Patient-delivered partner-therapy should be offered to all patients diagnosed and treated for NGU. Patients should be encouraged to additionally refer partner(s) in the past 60 days for evaluation. A specific diagnosis may facilitate partner referral; therefore, testing patients with NGU for both gonorrhea and chlamydia is recommended.

Recurrent and Persistent Urethritis

In addition to symptoms reported by the patient, objective signs of urethritis should be confirmed by the clinician before initiation of antimicrobial therapy. Effective regimens have not been identified for treating patients who have persistent symptoms or frequent recurrences after treatment. Such patients should be re-treated with an alternate recommended regimen if it is possible they did not adhere with the treatment regimen or if they may have been re-exposed to an untreated sex partner. If re-infection is unlikely, treatment should be directed against other, less common causes of urethritis.

In addition, there is increasing evidence that oral sex can be associated with NGU, and that Herpes Simplex Virus, adenovirus and normal oral flora may also be causative organisms. Some of these causative organisms do not have specific treatment and may also contribute to recurrent urethritis.

A. Evaluation

1. Verify diagnosis of urethritis by presence of discharge and microscopic evaluation of urethral swab, by leukocyte esterase urine test, or examination of urine sediment.
2. If the patient has persistent urethritis and is believed to have correctly completed a recommended regimen, has had his partner(s) treated appropriately, and denies re-exposure, the following regimen is recommended:

Recommended Treatment for Recurrent/Persistent Urethritis:

1. **Azithromycin** 1 g orally once or
2. **Doxycycline** 100 mg BID x 7 days

Use whichever regimen (azithro or doxy) not given previously plus,

Metronidazole 2 g orally once for possible trichomonas infection in men who have sex with women.

Can consider a trial of treatment for HSV (see section on urethritis) confirm with HSV PCR of urethral meatus

Acyclovir 400mg tid x 5 days for initial episode (see section on anogenital herpes for complete list of treatment regimens).

B. Counseling/Education

Patients should:

1. Be counseled about urethritis.
2. Understand how to take prescribed oral medications.
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination and treatment.

5. Avoid sex for at least 7 days and until partner(s) are treated (include the period when both partners are taking medication).
6. Use condoms to prevent future infections.

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. Condoms should be used to decrease transmission.
5. It is important for female partners to be examined as pathogens may be more easily identified in the partner (e.g. trichomonas).

C. Sexual Behavior

1. Patients should be instructed to refrain from having sex with their partner(s) until both they and their partner(s) have completed taking all of their medication. Some patients think that it is safe to have unprotected sex if both they and their partner(s) are taking medication simultaneously. The risk of re-infection needs to be explained. Even if a one-time dose of medication is prescribed patients need to be instructed to avoid sex for 7 full days.
2. If a patient decides to have sex before completing their medication, instruct them to always use a condom. Remind the patient that condoms can break.
3. Patients should be advised to confirm/verify that their partner(s) have been adequately treated before engaging in unprotected sex with that partner again.
4. Patients should be informed that oral sex can cause urethritis due to bacteria or viruses in the mouth of their partners, which may not be typical sexually transmitted organisms. There are no commercially available tests for most of these organisms, and no specific treatment, but symptoms are usually self-limited.

PAP Smear Collection

Cervical Cancer Screening For Women Who Attend STD Clinics Or Have A History of STDs

Women who have a history of a STD are at increased risk for cervical cancer, and women attending STD clinics may have additional characteristics that place them at even higher risk. Prevalence studies have found that precursor lesions for cervical cancer occur about five times more commonly among women attending STD clinics than among women attending family planning clinics.

The Papanicolaou (Pap) smear (cervical smear) is an effective and relatively low-cost screening test for invasive cervical cancer and squamous intraepithelial lesions (SIL), the precursors of cervical cancer. The screening guidelines of both the American College of Obstetricians and Gynecologists (ACOG) and the American Cancer Society (ACS) recommend Pap smears every 12 months for all sexually active women, age 20-30. Although these guidelines take the position that Pap smears can be obtained less frequently in women age > 30 years, women with a history of STDs may need screening more frequently because of their increased risk for cervical cancer. Moreover, studies conducted among women attending STD clinics indicate that many women do not understand the importance of Pap smears and almost half of women who have had a pelvic examination erroneously believe they had a Pap smear when they actually have not.

A. Recommendations

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

1. Purpose and importance of a Pap smear.
2. Whether a Pap smear was obtained during the clinic visit.
3. Need for a Pap smear at least every 12 months.
4. Offer to perform a Pap smear at this visit if it has been more than a year since last done, or if pt has missed a follow-up for a previously abnormal Pap.

Women “out of the care loop”, psychiatric patients, and homeless women should probably have a Pap done on an STD visit while there is an opportunity to do it, regardless of their place in the menstrual cycle or possible concurrent STDs. (Clinician discretion)

It is important not to miss opportunities to perform Pap smears in these high-risk patients when they present to STD clinic.

B. Other Management Considerations

Other considerations in performing Pap smears are the following:

1. The Pap smear is not an effective screening test for STDs. If indicated, other diagnostic testing for STDs should be performed (see below).
2. If a woman is menstruating, a Pap smear should ideally be postponed and the woman should be advised to have a Pap smear at the earliest opportunity (Clinician discretion – see previous note).
3. The presence of a mucopurulent discharge may compromise interpretation of the Pap smear. However, if the woman is unlikely to return for follow-up, a Pap smear can be obtained after gentle removal of the discharge with a large cotton swab (Scopette).
4. A woman with external genital warts does not need to have Pap smears more frequently than a woman without warts, unless otherwise indicated.
5. In an STD clinic setting or when other cultures or specimens are collected for STD diagnoses, the Pap smear may be obtained last.
6. Women who have had hysterectomies do not require annual Pap smears unless the hysterectomy was related to cervical cancer or its precursor lesions. In this case, women should be advised to continue follow-up with the physician(s) involved in their care at that time.
7. Healthcare providers who receive basic retraining on Pap smear collection and clinics using simple quality assurance measures obtain fewer unsatisfactory smears.

C. Colposcopy

City Clinic provides colposcopy to women who are in the Family Planning Program (Medi-Cal Family PACT). Women needing colposcopy who are not in the Family Planning Program or who do not have Medi-Cal should be referred to the SFGH Dysplasia Clinic. These women should be evaluated with one of the clinicians in the Family Planning Program.

D. Special Considerations

Pregnancy:

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

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. There are approximately 1 million cases in the US per year. PID may include endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Sexually transmitted organisms, especially *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, are implicated in most cases, but *Mycoplasma genitalium* has been increasingly recognized as a cause of PID. In addition, bacteria not usually associated with sexual transmission, such as anaerobes, Gram-negative rods and streptococci may also be etiologic agents.

Many women with PID have no symptoms or just mild-to-moderate lower abdominal pain and tenderness; indeed, many women with late complications of PID (e.g., infertility, ectopic pregnancy) report no known history of PID. Occasionally, acute infection 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, pelvic adhesions requiring subsequent surgery, and psychological depression.

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

A. Diagnosis

The clinical diagnosis is imprecise but should always be considered in women with cervical, uterine or adnexal pain. Health care providers should maintain a low threshold for making the diagnosis of PID.

1. History:

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

2. Examination:

- a. Check temperature in patients suspected of having PID.
- b. Complete pelvic exam should be performed to assess for cervical, uterine or adnexal tenderness.

- c. Peritoneal signs (rebound, guarding) or right upper quadrant tenderness (possible Fitz-Hugh-Curtis syndrome) may be present.
3. Laboratory:
 - a. Perform pregnancy test in all patients with suspected PID.
 - b. ⊕ Wet prep of vaginal secretions (see criteria below).
 - c. Gram stain of cervical discharge to look for white blood cells and gonococci.
 - d. Test for gonorrhea and chlamydia, and syphilis.
4. Empiric treatment of PID should be initiated in sexually active young women and other women at risk for STDs if the following minimum criteria are present:
 - a. Lower abdominal pain **and**
 - b. Cervical motion tenderness **or** Uterine tenderness **or** adnexal tenderness.
 - c. Absence of other causes of pelvic pain (e.g., ectopic pregnancy, appendicitis).
5. Additional criteria useful in diagnosing PID:
 - a. Oral temperature >38.3 C (101 F).
 - b. Abnormal cervical or vaginal discharge.
 - c. Presence of white blood cells (WBCs) on saline microscopy of vaginal secretions.
 - d. Evidence of cervical infection with *N. gonorrhoeae* or *C. trachomatis*.
6. Other diagnostic criteria (not available at City Clinic):
 - a. Elevated erythrocyte sedimentation rate or CRP.
 - b. Histopathologic evidence on endometrial biopsy.
 - c. Tubo-ovarian abscess on sonography or CT scan.
 - d. Characteristic findings on laparoscopy.
7. Evaluate for Bacterial Vaginosis
 - a. Obtain vaginal pH.
 - b. Evaluate clue cells and wet mount.
 - c. Characterize discharge.
 - d. Evaluate whiff test.

B. Treatment

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

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

a. Regimen A

1. **Ceftriaxone** 250 mg IM once **and**
2. **Doxycycline** 100mg PO BID for 14 days
with or without

If patient is diagnosed with Bacterial Vaginosis, treat with:

1. **Metronidazole** 500 mg PO BID for 14 days

b. Regimen B

1. **Ofloxacin** 400 mg PO BID for 14 days (not available at City Clinic), and
2. **Doxycycline** 100 mg PO BID for 14 days

Alternative Oral Regimens

Information regarding other outpatient regimens is limited, but one other regimen has undergone at least one clinical trial and has broad-spectrum coverage. Amoxicillin/clavulanic acid plus doxycycline was effective in obtaining short-term clinical response in a single clinical trial; however gastrointestinal symptoms might limit the overall success of this regimen. Several recent investigations have evaluated the use of azithromycin in the treatment of upper-reproductive tract infections; however, the data are limited. Ceftriaxone plus azithromycin instead of doxycycline is an option in potentially non-adherent patients; the suggested dose is azithromycin 1 gram PO x 1 followed by a second 1 gram dose one week later.

2. Hospitalization is recommended in the following situations*:

- a. Surgical emergencies such as appendicitis or ectopic pregnancy cannot be excluded.
- b. A pelvic abscess is suspected.
- c. The patient is pregnant.
- d. Patient compliance is uncertain.
- e. Severe illness precludes outpatient management (e.g., Temp >38.3C, moderate or severe dehydration, vomiting, peritoneal signs present).
- f. The patient has failed to respond to outpatient therapy (defined below).

*If the patient is referred for evaluation to SFGH ER, treatment should be instituted before patient leaves SF City Clinic as failure to follow-up at SFGH ER is often a problem.

C. Follow-up

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

Follow-up at three days should establish:

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

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

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

D. Counseling/Education

Patients should:

1. Be counseled about the risks of PID and routes of transmission.
2. Understand how to take prescribed oral medications.
3. Return three days after initiation of therapy for repeat evaluation.
4. Return for examination four to seven days after completing therapy.
5. Receive patient delivered therapy for GC/CT and refer sex partner(s) for examination and treatment.
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. Use condoms to prevent future infections.
9. Understand the health risks of current and future episodes of PID.
10. Advised to seek care at an ER if there is sudden worsening of symptoms and SFCC is not open.

E. Evaluation of Sex Partners

Patient-delivered therapy for *C. trachomatis* and *N. gonorrhoeae* should be given for all partners in the past 60 days. Partners should also be referred for evaluation for other STDs.

F. Special Considerations

Intrauterine device: The benefit of removing an IUD in PID in terms of response to antimicrobial therapy and the risk of recurrent PID is not fully established. In compliant patients with uncomplicated PID, the IUD may be left in place during antimicrobial treatment if the woman desires to continue with the IUD as a contraceptive method. Reinforce with the patient that this approach requires close follow up with a repeat exam in 2 to 3 days. If 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. This protocol will only present the diagnostic workup and treatments for proctitis. Since the DPH lab no longer processes stool kits for ova, parasites, and bacteria for City Clinic patients, all patients who present with enteric symptoms (diarrhea, abdominal cramps, etc.) should be referred to the San Francisco General Hospital Emergency Room, Tom Waddell Clinic, district health centers, or their private providers.

Proctitis is inflammation limited to the rectum and is associated with anorectal pain, tenesmus, and discharge. *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Herpes Simplex Virus* types I and II and syphilis are the most common sexually transmitted pathogens involved.

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

A. Diagnosis

1. History:
 - a. Patients present with symptoms referable to the rectum: rectal pain, tenesmus, and discharge.
 - b. Patients usually have a past or recent history of receptive anal intercourse.
2. Examination:
 - a. Using anoscope, look for rectal discharge, rectal ulcerations, perianal vesicles or ulcers.
3. Laboratory:
 - a. Gram stain rectal discharge from anoscopy.
 - b. Obtain rectal gonococcal NAAT or culture.
 - c. Obtain a chlamydia NAAT.
 - d. Obtain a herpes culture or HSV PCR even if no obvious lesions are present.
 - e. Serum VDRL.
 - f. HSV-2 serology, if no prior record.
4. Diagnostic criteria:
 - a. A positive rectal gonorrhea, chlamydia or herpes test or history of rectal contact to a patient with gonorrhea, chlamydia, or NGU and compatible symptoms and signs. Gram-negative intracellular diplococci or any WBCs on

Gram stain of rectal discharge provide good presumptive evidence of proctitis.

B. Treatment

Treatment should cover *N. gonorrhoea* and *C. trachomatis*. Consider additional empiric treatment for HSV if clinical suspicion is high (important to send HSV PCR for confirmation).

1. **Cefpodoxime** 400 mg PO x 1 and
2. **Doxycycline** 100 mg orally BID for seven days (or azithromycin 1 gm PO x 1)
or
3. **Ceftriaxone** 125 mg IM (with co-treatment for CT as above) and
4. **Acyclovir** 400 mg orally TID for 7 days for HSV infection

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 recurrence in these individuals.

D. Counseling/Education

Patients should:

1. Understand how to take prescribed medication.
2. Refer their sex partners for evaluation.
3. Avoid rectal intercourse x 7 days, and then only with condoms.
4. Avoid receptive anilingus x 7 days, and
5. Patients with rectal GC and other forms of proctitis should be counseled about their HIV risk and tested for HIV. HIV negative individuals may be referred to the Options project at SFGH (502-8100) for further HIV evaluation and/or to City Clinic Prevention Case Management. HIV positive clients with proctitis should be counseled about their increased infectiousness to anal insertive partners who are HIV negative.
6. Patients should repeat HIV testing at 3 months.

E. Evaluation of Sex Partners

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

Pubic Lice (Crabs)

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

A. Diagnosis

1. History:
 - a. Patients generally present with pruritus in the pubic region.
 - b. Often, patients have been able to visualize the lice or the nits.
2. Examination:
 - a. The pubic hair should be carefully examined for the presence of lice and/or nits.
 - b. Excoriation may be present but otherwise the skin should appear normal.
3. Laboratory:
 - a. 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.
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

Any of the following regimens are effective; only lindane requires a prescription. All treatments should be followed by combing the affected area with a fine-toothed comb – this step is critical because it removes eggs that would otherwise hatch and prolong infestation. Do not use for infestation of the eyelashes; see Section F, Special considerations for recommended treatment.

1. Permethrin (1%) creme (Nix) rinse applied to the affected area and rinsed off in 10 minutes. 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.

C. Other Studies

Pubic lice are an STD, so the patient should be evaluated and appropriate tests for other STDs ordered at the initial visit.

D. Follow-up

Patients should be re-evaluated after one week if symptoms persist. Re-treatment may be necessary if lice are found or nits are observed at the hair-skin junction.

E. Counseling/Education

Patients should:

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

F. Evaluation of Sex Partners

Individuals with sexual, household or close physical contact should be referred for treatment.

Patient delivered partner therapy (PDPT) should be offered for current or recent partners.

G. 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*, usually penetrates the skin, creating visible papules, or small, linear burrows, which contain the mites and their eggs. Common sites of infection include the flexor surface of the wrists, webbing between fingers, anterior axillary folds, the inner aspects of the upper thigh, and the belt line. Nodules appearing on the scrotum and penis typically are large. Scabies is rarely found on the head in adults. Two to six weeks after infection, pruritus (which is usually worse at night) begins. The itching represents a hypersensitivity reaction to the mite and will persist even after mites are dead. Individuals with a prior history of scabies may have more rapid onset of symptoms due to prior sensitization. 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. The rash is generally bilaterally symmetrical.
 - b. Excoriations may be present; some may be secondarily infected.
3. Laboratory:
 - a. Although the mite can at times be extruded from a burrow, this requires a fair amount of experience and is not necessary to make a diagnosis. Scrape linear skin lesion with scapel with oil on it so skin scrapings stay on scapel. Roll onto slide - examine under low and high power look for mite, eggs or feces of mite. Hand lesions are more likely to be positive.
 - 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), or common sites.
 - c. Sexual exposure or close physical contact to a person infested with scabies mites.
 - d. Exclusion of syphilis, if necessary.

B. Treatment

1. Elimite cream or Acticin cream (5% permethrin) applied from the neck down and washed off after 8-12 hours. Repeat application as above after one week if patient is still symptomatic. Medication comes in a 60 gram tube and is not contraindicated in pregnancy or during lactation. Patients should be informed that pruritus may persist for 1-3 weeks after therapy.
2. The presence of lindane-resistant scabies makes Kwell (1% lindane) a secondary therapeutic choice. Lindane is contraindicated in pregnant or lactating women.

C. Follow-up

A second treatment may be indicated for HIV infected individuals a week later with either of the two medications. They should be re-checked in 2 weeks.

D. 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.

E. Evaluation of Sex Partners

All sex partners and household contacts of patients who have scabies infection should be promptly treated.

Patients with scabies should be offered patient delivered partner therapy (PDPT) to take to partners.

F. 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.

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 characterized by a painless, indurated ulcer (chancre) that appears at the site(s) of infection by *T. pallidum* in about 21 days (the range is 10-90 days) and lasts from one to five weeks. The inguinal lymph nodes may become mildly to moderately enlarged but are minimally tender.

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

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

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

Neurosyphilis may occur at any stage of the disease; it may be symptomatic or asymptomatic. Neurosyphilis remains a clinical diagnosis since there is no commercially available test that is both highly sensitive and specific for it. 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.

There is another category of syphilis; **latent syphilis of unknown duration**. This diagnosis should be made in a patient between the ages of 13 and 40 who presents with a VDRL titer of 1:32 or greater, no previous reactive serologic test for syphilis, and a negative exam. In general titers correlate with disease activity so it is reasonable to suspect that the patient who fits the category of latent syphilis of unknown duration has early disease, but there is no way to be absolutely certain. Patients with syphilis of unknown duration should be treated with the treatment regimen for late latent disease, but interviewed for partner notification purposes for the previous year as for early latent syphilis (see section E).

Syphilis in Special Populations

Diagnostic Considerations:

HIV-Infected Persons:

Unusual serologic responses have been observed among HIV-infected individuals who are coinfecting 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 non-treponemal serologic tests for syphilis are accurate for the majority of patients with syphilis and HIV coinfection.

Pregnancy:

Because congenital syphilis is a serious disease, special precautions must be taken with women of childbearing age and pregnant women with syphilis. All women diagnosed with any stage of syphilis must have a stat urine pregnancy test. If the test is positive, she must be counseled concerning syphilis and pregnancy. If she chooses to continue her pregnancy, a prenatal care appointment should be made for her.

A. Stages of Syphilis

Primary syphilis

1. History:

- a. Patients may present with a genital, anal, or oral ulcer, called a chancre; classically this is 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. HIV positive individuals are more likely to have multiple ulcers.
- b. Patients should be questioned regarding neurologic symptoms. Patients with early syphilis may have acute syphilitic meningitis and may present with headache, fever, photophobia, neck stiffness, nausea, vomiting, papilledema, seizures, aphasia, hemiplegia, and cranial nerve palsies (including hearing loss). Any neurologic symptom may be consistent with 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. Note that multiple chancres are more likely in HIV positive individuals.
- d. Chancres may be atypical: for example they may lack induration, have flat rather than rolled edges, and be painful.
- e. A neurological exam should be performed. If there are symptoms or signs suggestive of neurosyphilis, the patient should be referred to SFGH Emergency Department for CSF analysis, evaluation and treatment. If the

patient has insurance and a primary care provider the patient can follow up there for the neurosyphilis evaluation. It is appropriate to call that provider with the patient's permission to facilitate this follow up. The Attending Physician should be notified of possible neurosyphilis cases.

3. Laboratory:

- a. A darkfield microscopic exam of the ulcer should be done. Do not perform darkfield on oral cavity lesions because exams at this site are difficult to interpret due to the presence of other non-pathogenic spirochetes. Lesions on the lips may be successfully evaluated with the darkfield exam.
- b. All ulcerative lesions should be swabbed for HSV PCR. At present the public health lab does not perform culture for *H. ducreyi* (the agent of chancroid).
- c. All patients must have a stat RPR, except for those with a positive darkfield exam. A VDRL and TPPA should always be done, even with a positive darkfield.
- d. Because syphilis is associated with an increased risk of HIV infection, HIV counseling and testing should be strongly encouraged. Rapid HIV testing should be performed, if available.
- e. Patients who have neurologic symptoms or signs should have a lumbar puncture as outlined above. CSF should be sent for cell count, differential, CSF VDRL, protein and glucose.

4. Diagnostic criteria:

Table of Syphilis Tests

Non-Treponemal/Screening*	Treponemal/Confirmatory
RPR VDRL	TP-PA FTA-ABS

*Individuals with reactive non-treponemal tests and non-reactive treponemal tests are considered to be biologic false positives (BFP). They do not have syphilis and do not require treatment.

- a. Darkfield microscopy is a highly sensitive method by which to diagnose primary syphilis (up to 95% sensitive in experienced hands); nontreponemal tests may be nonreactive in the primary stage (70-75% sensitivity) for up to 10 days after the appearance of the chancre. Among treponemal tests in untreated primary syphilis, the FTA-ABS (90-95% sensitive) is first to become reactive, followed by the TP – PA (90 – 95% sensitive). Treponemal tests may become reactive earlier than non-treponemal tests.

- b. Primary syphilis is characterized by typical lesion(s) with either a reactive nontreponemal (VDRL, RPR) test and no prior history of syphilis, or a fourfold or greater increase in titer on a quantitative nontreponemal test compared with the most recent test for persons with a history of syphilis.

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 corner 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 fields should be examined before determining that spirochetes are not present; performing second and third darkfield exams on all lesions are 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.

(*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).

6. Many patients with genital lesions apply topical treatments to their lesions, which may produce a negative darkfield test.

Secondary Syphilis

1. History:

- a. Patients may present with a rash (may be on the genitals, the palms and soles, or generalized), patchy hair loss (moth eaten appearance), or white, grey or flesh-colored lesions in the oral cavity (mucous patches) or in the anogenital region (*condyloma lata*). The rash is rarely pruritic and is never vesicular.
- b. Constitutional symptoms may be present, especially in HIV positive persons. Question regarding history of fever, headache, increased fatigue, sore throat, or night sweats.
- c. Be sure to ask the patient about recent sores in genital, oral, and anal regions, and swollen lymph nodes.
- d. Patients should be questioned regarding neurologic symptoms. Patients with early syphilis may have acute syphilitic meningitis and may present with headache, fever, photophobia, neck stiffness, nausea, vomiting, seizures, dizziness, focal weakness, trouble speaking, changes in hearing, or vision.

2. Examination:

- a. A complete exam including the oral cavity (mucous patches, chancre), anogenital region (*condyloma lata*, chancres, mucous patches), and the neck, chest, inguinal area, axilla and forearms (adenopathy) should be done. Any rash on the genitals, especially the scrotum should be suspect for syphilis.
- b. The rash of secondary syphilis is bilaterally symmetrical, and can often be varied, presenting as maculopapular, or 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. If there are symptoms and signs suggestive of neurosyphilis, the patient should be referred to the SFGH Emergency Room for lumbar puncture.

Laboratory:

- a. Moist lesions of secondary syphilis (eg. *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 for CSF analyses, including VDRL, protein, glucose, WBC, and RBC.

3. Criteria for Clinical Diagnosis of Secondary Syphilis:

- a. Identification of *T. pallidum* from material from cutaneous or mucous membrane lesions by darkfield microscopy.
- b. Reactive nontreponemal (VDRL, RPR) 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, ie VDRL for both, or RPR for both) and any one of the following skin or mucous membrane lesions of secondary syphilis:
 1. skin lesions (bilaterally symmetrical, macular, papular, follicular, papulosquamous, or pustular). There may also be lesions on the face known as nickel and dime lesions (annular syphilids) or split papules in the nasolabial folds 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 or cervix.

4. alopecia of head hair or 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 with special attention to discover signs of primary or secondary syphilis.
- b. A neurological exam should be performed. If there are symptoms and signs suggestive of neurosyphilis, the patient should be referred to the SFGH Emergency Department for lumbar puncture.

3. Laboratory:

The only laboratory evidence of latent syphilis is a reactive VDRL (or RPR) with a positive TP – PA (or FTA-ABS).

4. Diagnostic criteria:

- a. Absence of symptoms and signs of primary or secondary syphilis with reactive nontreponemal (VDRL, RPR) and treponemal tests in a patient with no prior history of syphilis and documentation of a nonreactive nontreponemal test during the past year.
- b. In a patient with a history of syphilis who has a fourfold or greater increase in titer on the nontreponemal (VDRL, RPR) test compared with the prior test performed within the past year.
- c. Patient who is asymptomatic and is a contact to early syphilis or syphilis of undetermined stage and who has a reactive VDRL (or RPR) and no prior history of syphilis.

Late Latent Syphilis

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

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.

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. If there are symptoms and signs suggestive of neurosyphilis, the patient should be referred to SFGH ED for lumbar puncture.

3. Laboratory:

- a. The only laboratory evidence of latent syphilis is a reactive VDRL (or RPR) with a positive TP – PA. On occasion the non-treponemal test may be non-reactive.
- b. CDC recommends that lumbar puncture be done in late latent syphilis if a patient has any of the following:
 - 1. Neurologic or ophthalmologic symptoms or signs
 - 2. Evidence of active disease, such as aortitis, gumma, or iritis
 - 3. Treatment failure
 - 4. HIV infection

If patients consent to lumbar puncture, inform the Attending Physician who can assist with scheduling. Lumbar punctures are generally done at SFGH Emergency Department. In general, benzathine penicillin therapy is often initiated prior to LP, but LP should be done as soon as possible.

4. Diagnostic criteria for Late Latent Syphilis:

- a. Absence of symptoms and signs with either a reactive treponemal test in a patient with no prior history of syphilis and no documentation of a nonreactive 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.
- c. A positive treponemal test in a patient without a prior history of syphilis.

If the patient is 40 years old or less and the VDRL titer is above 1:32 or the patient is designated as having latent syphilis of unknown duration.

There must be a documented positive treponemal test before therapy is started. This will assure that patients with biologic false positive nontreponemal tests for syphilis don't get treated for a disease they don't have.

Neurosyphilis

Can occur at any stage of disease.

1. History:

- a. Patient's with acute syphilitic meningitis or meningovascular syphilis (usually occurs in patients with early syphilis) may complain of headache, fever, photophobia, neck stiffness, nausea, vomiting, blurred vision, seizures, aphasia, focal weakness, hemiplegia, cranial nerve palsies (including hearing loss). Patients with general paresis or tabes dorsalis may present with dementia, psychosis, gait disturbances, lightning pains, or incontinence.

2. Examination:

- a. Patients may have no neurologic abnormalities.
- b. Neurologic deficits as suggested above may occur with early or late disease.

3. Laboratory:

Diagnostic criteria:

- a. Abnormal CSF WBC > 5 cells/ μ l; CSF protein > 40 mg/dl, or positive CSF VDRL*.
- b. Identification of *T. pallidum* in CSF or CNS tissue by PCR, animal inoculation, DFA, or histology (not done in routine clinical practice).

**Note that in HIV positive patients, there may be a mild elevation of CSF WBC due to HIV itself, so a more appropriate diagnostic criterion for neurosyphilis is 10 WBC/ μ l. Cases of suspected neurosyphilis should be discussed with the attending physician, or call 487-5595 for expert consultation.*

B. Treatment

1. Early Syphilis (less than 1 year duration)

- a. Benzathine penicillin 2.4 million units IM once.
- b. For nonpregnant patients who are penicillin-allergic or refuse penicillin therapy, doxycycline 100 mg orally BID for 14 days may be substituted.
- c. Pregnant women with early syphilis may only be treated with 2.4 million units of benzathine penicillin.
- d. HIV-infected individuals should be treated with benzathine penicillin 2.4 million units IM once.

2. Late Syphilis (greater than 1 year duration and of unknown duration)

- a. Benzathine penicillin 2.4 million units IM once each week for three weeks.
- b. For nonpregnant penicillin-allergic patients, doxycycline 100 mg orally twice daily for 30 days may be substituted. This should be given to patients in 2 two-week packets so that mid-point VDRL and clinical evaluation can be repeated to rule out early latent syphilis and to assess adherence with the therapy.

3. Contacts/Clusters

- a. Benzathine penicillin 2.4 million units IM once.
- b. Doxycycline 100 mg orally BID x 14 days non-pregnant patients who refuse penicillin or are penicillin allergic.
- c. Treatment may be given in the field by trained personnel.

Notes on treatment:

Pregnant patients with syphilis may ONLY be treated with penicillin. No other treatment should be given. Pregnant women with a history of true penicillin allergy should be seen by the Attending Physician and referred for desensitization and treatment. The UCSF Immunology fellow should be paged to arrange evaluation.

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

Patients who are receiving three doses of penicillin must restart their treatment if more than 10 days elapse since the last dose. They should also receive each dose no sooner than five days since the preceding one.

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 return for examination one week, 1 month, 2 months, 3 months, 6 months, 9 months, and 12 months after treatment. At the initial follow-up visit be sure to document a patient's report of a Jarisch-Herxheimer reaction and document the healing of lesions, diminution in extent of rash, etc. At all syphilis follow-up visits patient should be asked about any new neurological symptoms. If patients have neurological symptoms, they should be evaluated and referred promptly.
- b. Repeat VDRL titers should be done at 1 month, 2 months, 3 months, 6 months, 9 months, and 12 months after diagnosis.
- c. Pregnant patients should be evaluated monthly and should have a complete obstetric history documented at the initial visit to determine if there are other children who may have congenital syphilis. If this is a possibility, the City Clinic surveillance unit should be notified.
- d. If nontreponemal antibody titers have not declined fourfold by 12 months for secondary and early latent syphilis, or if they increase fourfold, the patient

should be evaluated for reinfection or neurosyphilis and should be treated accordingly. The Attending Physician should be consulted for such cases.

2. Late Syphilis

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

D. Counseling/Education

Syphilis cases should:

1. Be referred to a DCI for counseling, clustering and names of partner(s); inform the DCI staff of all cases of latent syphilis of unknown duration so that the DCI can interview the patient as they would an early latent case. (Name partner(s) for the past year).
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. Use condoms to prevent future infections.
8. Understand that syphilis has been associated with an increased risk of HIV transmission and that City Clinic strongly urges syphilis patients to be HIV tested.
9. Understand that in individuals with prior, known HIV-infection, syphilis may increase HIV viral load and therefore increase HIV transmission risk to an HIV-negative partner. It may also decrease CD4 count in HIV infected patients not treated for HIV.

E. Evaluation of Sex Partners

All sex partners of patients with early syphilis and syphilis of undetermined stage should be evaluated clinically and serologically, and should receive treatment that is appropriate to the results of their evaluations. **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.** Contacts to patients with syphilis of undetermined stage must be managed in the same manner as contacts to early disease. Therefore, it is imperative to carefully review the case of the index patient. Contacts to patients with true late latent disease and who have a negative stat RPR need not be treated. All contacts to syphilis should have a stat RPR done unless they are known to be serofast: this occurs when a person with past treated syphilis and a documented treatment history has persistently reactive RPR or VDRL titers. These titers tend to be 1:8 or lower but may be higher. In this case obtain a VDRL and treat presumptively if the contact was within the 90-day incubation period. 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.

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. Use condoms to prevent future infections.

Understand that syphilis has been associated with an increased risk of HIV transmission and that City Clinic strongly urges syphilis patients to be HIV tested.

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

F. Evaluation of Clusters/Social Sexual Network Contacts

All clusters named by patients with early syphilis, contacts to early syphilis, and syphilis of undetermined stage should be evaluated clinically and serologically, and should receive treatment that is appropriate to the results of their evaluations.

Clusters include the following individuals:

1. Suspects: A person named by the original infected syphilis patient (OP) during an interview, who is not the OP's sex partner.

Suspects are divided into three groups:

S-1: has symptoms suggestive of syphilis, such as a rash or a genital sore,

S-2: is a sex partner of *another* person known to be infected with syphilis, and

S-3: does not fit in either of the other categories, but needs an exam because they are at high risk of exposure to syphilis such as a person who has unprotected anal sex with anonymous partners.

2. Associates: A person named by someone involved in a syphilis case, who is not infected, such as a contact to syphilis with a negative RPR.

Associates are also divided into three groups:

A-1: has symptoms suggestive of disease,

A-2: is a sex partner of a person known to be infected, and

A-3: does not fit in either of the other categories, but needs an exam because they are at high risk of exposure to syphilis such as a person who has unprotected anal sex with anonymous partners.

Exposure dates for S2's and A2's may not be available. For this reason, they should be assumed to be a contact to early syphilis within 90 days of diagnosis and be presumptively treated, regardless of reported sexual history.

All clusters to early syphilis should have a stat RPR done unless they are known to be serofast. In this case obtain a VDRL and treat presumptively if the person is classified as an S2 or A2. Clusters whose RPR is reactive should be diagnosed as having syphilis, staged, and be treated appropriately. If the RPR is nonreactive and the person is classified as an S1, A1, S3 or A3, prophylactic treatment is not necessary.

Note: If there are any questions concerning any aspect of syphilis diagnosis, treatment, follow-up, LP, etc., ask the Attending Physician for advice.

Trichomoniasis

Trichomoniasis is a sexually transmitted infection caused by the single-celled protozoan parasite *Trichomonas vaginalis*. Female patients may be asymptomatic, or they may present with itching and malodorous vaginal discharge. Male sex partners are usually asymptomatic, but urethritis may develop. There is a strong association with other STDs, particularly gonorrhea, so STD screening is indicated. There may be an association between trichomoniasis and adverse pregnancy outcomes, particularly premature rupture of the membranes and preterm delivery.

A. Diagnosis

1. History:
 - a. Patients may be asymptomatic.
 - b. If symptomatic, patients typically present with a malodorous vaginal discharge and vaginal itching.
 - c. Men may present with dysuria or penile discomfort.
2. Examination:
 - a. Profuse, malodorous frothy, gray 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. Culture using the InPouch TV culture system may be done for trichomonads in the SFCC on-site lab when the diagnosis is in question.
4. Diagnostic criteria:
 - a. 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.
 - b. Identification of *T. vaginalis* by InPouch culture system.
 - c. 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

Primary

1. **Metronidazole** 2 grams PO once.
2. **Tinidazole** 2 grams PO once (costly).

Recurrence

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

1. If re-infection is likely, retreat with primary regimens above.
2. Patients who fail to respond to single dose therapy should be retreated with **Metronidazole** 500 mg PO BID for seven days.
3. Patients who fail with the 7-day therapy should be treated with **Metronidazole** 2 grams PO qd for five days.
4. Recalcitrant or possible metronidazole resistant trichomonas infections (i.e. wet-mount confirmed trichomoniasis after escalating dose regimens listed above) can have trichomoniasis confirmed by culture, using the In-Pouch TV. Culture can be obtained from vaginal specimen or a spun urine sediment. The culture can be sent to the CDC for resistance testing (see procedure manual, Patient Evaluation for Possible Resistant Trichomoniasis).

Other treatment alternatives for resistant trichomoniasis include:

1. Paramomycin vaginal inserts 250mg x 7-14 days and metronidazole 500mg QID x 7-14 days (see procedure manual for compounding pharmacy info) (very costly).
2. Furazolidone (Furoxone) orally or topically – not available at SFGH.
 - a. Furazolidone 8.8mg/kg/day in 4 divided doses x 3 days (approximately 400mg/day for a 45 kg person – 100mg QID x 3 days) (very costly).
 - b. For topical formulation, consult Procedure manual.

C. Follow-up

Routine follow-up is not required.

D. Counseling/Education

Patients should:

1. Be counseled about the sexual transmission of trichomoniasis.
2. Understand how to take or use prescribed medications (e.g., alcohol should be avoided during and for 24 hours after treatment with metronidazole).
3. Return for evaluation if symptoms persist or recur after treatment.
4. Refer sex partner(s) for examination for other STD and treatment.

5. Avoid sex for at least 7 days after patient AND partner(s) are treated.
6. Use condoms to prevent future infections.
7. Know that males frequently are asymptomatic even if infected.
8. Know that trichomoniasis, like other STDs, increases the risk of HIV transmission.

E. Evaluation of Sex Partners

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

Sex partners should also be screened for gonorrhea, chlamydia and syphilis and counseled as above.

Urinary Tract Infections

Urinary tract infections (UTI) may be limited to the lower urinary tract (cystitis) or may include both the upper and lower tracts (pyelonephritis). The most common uropathogen is *Escherichia coli* (80-85%), followed by *Staphylococcus saprophyticus*, a Gram-positive organism. Gram-negative rods including *Proteus mirabilis*, *Klebsiella pneumoniae*, and others are less common uropathogens. Uropathogens originate primarily from the bowel. Lower urinary tract infections appear to be limited to the mucosal surfaces of the lower urinary tract, which makes them relatively easy to cure with a short course of antimicrobial therapy. Symptoms generally include pain with urination, frequency, and urgency. These symptoms may occur from urethritis in the absence of bladder infection. Therefore, it is important to distinguish between urethritis (i.e., Gonorrheal or Chlamydial urethritis) and cystitis, particularly in a sexually active population.

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

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

A. Diagnosis

1. History:

- a. Patients often present with acute onset (less than 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 and fever.
- c. Any history of chronic or recurrent UTIs or UTIs with a resistant organism as well as risk factors (e.g. diabetes, use of diaphragms) should be elicited.
- d. Take a thorough sexual history because urethritis and vaginitis can have a similar presentation. A recent new partner should raise suspicion of STD, and not necessarily a UTI, although UTIs can be associated with inadequate emptying of bladder and with intercourse (“honeymoon cystitis”).

2. Examination:

- a. There may be suprapubic tenderness.
- b. A careful evaluation for flank (costovertebral angle) tenderness (CVAT) must be done. If present, take the patient's temperature.
- c. A pelvic exam to rule out vaginitis, cervicitis, and other STD is an important part of the evaluation. Test for chlamydial and gonococcal infection by vaginal swab.
- d. 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.

3. Diagnostic Criteria:

- a. A midstream clean catch urine may be tested for leukocyte esterase and nitrite production by a dipstick. 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 urine should be centrifuged and a drop of the sediment should be evaluated under the high dry objective. The presence of >10 WBCs per HPF 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. The patient should have a negative pelvic exam except for possible bladder wall tenderness.
- e. Urine culture and sensitivity should be ordered if a patient does not respond to therapy, has pyelonephritis, has recurrent infections, or is male.

B. Treatment

Uncomplicated lower UTI (cystitis)

1. May be treated with short course therapy.
2. Does not require urine culture prior to treatment.
3. Patients should follow-up if symptoms recur, persist, worsen and/or signs or symptoms of upper tract involvement occur.

Treatment (non-pregnant)

1. **TMP-SMX** PO BID for 3 days, or
2. **Nitrofurantoin** (Macrobid) 100 mg PO QID for 7 days, or
3. **Ciprofloxacin** 250 mg PO BID for 3 days.

Treatment (pregnant)

1. **Nitrofurantoin** (Macrobid) 100 mg PO QID for 7 days, or
2. **Cephalexin** 500 mg PO QID for 7 days.

Fluoroquinolones such as Ciprofloxacin should not be used in pregnancy

Complicated lower UTI

1. Relapsing infection: occurs within two weeks of completion of therapy.
2. History of UTI with antibiotic resistant organism.
3. History of multiple serious antibiotic allergic reactions.
4. History of multiple UTIs >5(avoid TMP/SMX use).
5. Male with UTI.
6. Symptoms greater than 7 days.
7. Pregnancy.
8. Diabetes.
9. Recent hospitalization or instrumentation.
10. Other significant underlying medical conditions.

Treatment:

Must be tailored to patient history and presentation and typically requires a 7-14 day course of treatment – consult with the Attending Physician

Upper UTI (pyelonephritis)

Treatment:

Notify Attending Physician and hospitalize for:

1. Hemodynamically unstable (high pulse, low blood pressure)
2. Pregnant
3. Vomiting and unable to tolerate oral meds
4. Unlikely to adhere to outpatient regimen, or to follow up in clinic

Outpatient management – if do not meet criteria for hospitalization above:

1. Send urine culture
2. **Ciprofloxacin** 500mg PO bid x 14 days
3. Pt must return to clinic for repeat evaluation in 72 hours, 7 days and 14 days
4. Patient should be told to present to clinic or the Emergency Department if symptoms worsen or unable to tolerate oral meds.

Patient Delivered Partner Therapy (PDPT)

Effective clinical management of patients diagnosed with treatable STDs requires treatment of their sex partners as well. Since 2001, state law in California allows clinicians to provide additional courses of STD treatment for partners of patients.

There have been three randomized controlled clinical trials that demonstrate that partner treatment reduces rates of repeat infection in the original patient. The CDC supports PDPT, and recommendations for its use are incorporated in its 2006 STD Treatment Guidelines.

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

1. **Chlamydia**
2. **Gonorrhea**
3. **Non-gonoccal Urethritis (NGU)**
4. **Trichomonas**

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 (and any necessary equipment, such as a sterile container to mix azithromycin powder with water)
2. Instructions for taking the medication
3. An information sheet about the STD for which they are receiving treatment
4. Condoms
5. Cards for City Clinic and InSpot, an online partner-notification resource.

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

Events Requiring Attending Physician Notification

1. Patient must be sent to urgent care or the emergency department for further evaluation.
2. Pelvic examination cannot be conducted satisfactorily.
3. Uterine enlargement or pelvic masses are found on exam.
4. Acute salpingitis or acute abdomen in a pregnant patient.
5. First episode genital herpes is found in a pregnant woman.
6. Testicles are painful, tender, or enlarged.
7. The diagnosis is uncertain or disease is severe.
8. The patient has a history of multiple drug allergies and requires treatment.
9. Serious sign of adverse reaction to treatment occurs, such as anaphylaxis (angioedema, urticaria, bronchospasm, hypotension, pruritis), skin rash, or anxiety.
10. The needed STD treatment or procedure is not specified in the preceding protocols (e.g. drainage of a bubo).
11. A serious surgical problem such as acute abdomen or less acute problems such as hernia or varicocele is present.

Common Medications Used for STDs

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

Select STD Resources

San Francisco City Clinic website: updated alerts, fact sheets, epidemiology reports and an electronic copy of clinical protocols:

<http://www.sfcityclinic.org> then click on providers

California STD/HIV Prevention Training Center

<http://www.stdhivtraining.org/>

CDC STD and guidelines:

<http://www.cdc.gov/std/>

<http://www.cdc.gov/std/treatment/>