

SEXUALLY TRANSMITTED INFECTIONS

Debra Shearer, EdD, MSN, FNP-BC

GENERAL APPROACH

Description

- ▶ Sexually transmitted infections (STIs) are also known as sexually transmitted diseases.
- ▶ 20 million new infections annually in the United States
- ▶ On January 18, 2013, the Food and Drug Administration (FDA) announced a shortage of doxycycline, which is recommended for chlamydia, nongonococcal urethritis, epididymitis, and pelvic inflammatory disease, as well as an alternative treatment for syphilis when there is penicillin allergy. Tetracycline is not available.

Prevention

- ▶ Counsel the adolescent or adult patient regarding sexual abstinence, the only certain method of prevention; followed by mutual monogamy,
- ▶ Consistent use of the male latex condom is highly protective if used consistently and correctly (see Chapter 12).
- ▶ Use of female condoms and other barrier methods of contraception for women may be somewhat protective against some, but not all, STIs.
- ▶ Safer sex practices are aimed at reducing risk of HIV transmission for patients at highest risk through partner reduction and avoidance of certain practices (see Chapter 4).

Risk Assessment

- ▶ Risk assessments and screening tests help reduce the incidence of STI and must be done on every sexually active adult and adolescent patient.
- ▶ Adolescents are at a higher risk for STIs.
- ▶ Obtain accurate, detailed history from patients to determine risk for STIs. Most people do not know they are infected with STI and underestimate their own risk level. Ask specific questions regarding type of sexual exposure in “lay terms” in order to obtain accurate information. Maintain confidentiality by asking partners and parents to leave the room. No parental consent is needed for adolescents to seek treatment for STI; the age of consent for adolescents varies by state.
- ▶ High-risk factors for STI are current STI(s), including HIV and history of STI(s); multiple sexual partners (or a new partner); exchanging sex for money or drugs; drug user or partner of drug user; homosexual or bisexual men and their partners; and lack of consistent use of barrier contraceptives.

Screening

- ▶ Routine steps for all sexually active (ever) women and men:
 - ▶ Explain importance and context of screening, since many STIs are asymptomatic: “We review this information and screen all patients because many people with infections do not have symptoms and therefore have no idea that testing might be needed. Routine review is recommended by the CDC.”
 - ▶ Give prevention information and encourage wise decisions and prevention behavior.
 - ▶ Review personal history for high-risk behaviors.
 - ▶ Provide annual *Chlamydia* test for men and women ≤ 25 years (urine or swab).
 - ▶ Women age 21–29 should have a Pap test every 3 years.
 - ▶ Women age 30–65 should have a Pap test every 3 years and co-test for cervical cytology and high-risk human papillomavirus (HPV) every 5 years.
 - ▶ Provide annual gonorrhea test if in an area of high *Gonococci* (GC) prevalence and age ≤ 25 years.
 - ▶ If in an area with high syphilis prevalence and age ≤ 25 years, or high-risk behavior, initial syphilis serology.
- ▶ Routine steps for high-risk women and men should include offering and encouraging HIV testing, reviewing history, and providing hepatitis B vaccination.
- ▶ Patients with known STI exposure or symptoms should be cultured from areas of exposure or penetration (e.g., anal, vaginal, oral pharyngeal, penile, or urethral), then treated.
- ▶ Routine screening in < 25 years (high-risk) pregnant women in first trimester should include syphilis serologic test, hepatitis B antigen, GC; offer HIV test, Pap smear. Repeat screening for high-risk women in third trimester or at delivery: Syphilis, hepatitis B antigen, GC and *Chlamydia*, and bacterial vaginosis (BV).

Management

- ▶ Follow Centers for Disease Control and Prevention on treatment guidelines for gonococcal infections (including 2011 update) for evaluation and management of all STIs.

- ▶ With patients who are likely not to return for follow-up, consider empiric treatment with CDC-recommended one-dose regimen when appropriate.
- ▶ Patients treated for STI should be counseled to have their sexual partners evaluated and treated.
- ▶ Sexually active patients should be counseled regarding dual protection against unintended pregnancy and STIs. The male latex condom is effective in providing dual protection if used correctly.

RED FLAGS

- ▶ Consult, refer, or hospitalize with unusual presentation of STI; serious complication such as PID, pregnancy, HIV infection, recurrent infection, unable to tolerate oral medication, allergy to medication
- ▶ Refer to infectious disease specialist for pregnant women with hepatitis B virus (HBV), primary cytomegalovirus (CMV), primary genital herpes, or Group B streptococcal infection, and women with syphilis and allergic to penicillin.
- ▶ With STIs in pediatric or adolescent populations, suspect child abuse.
- ▶ If patient reports sexual assault, consult local law authorities regarding procedures for obtaining evidence. Test for *Trichomonas vaginalis*, bacterial vaginosis, yeast, *Chlamydia*, GC, HIV, hepatitis B, and syphilis. Empiric antimicrobial regimen for *Chlamydia*, gonorrhea, *Trichomonas*, and BV is suggested, as well as prophylactic treatment for Hep B, pregnancy testing, and emergency contraception, if indicated.

INFECTIONS THAT CAUSE VAGINITIS AND CERVICITIS IN WOMEN AND URETHRITIS IN MEN

TRICHOMONIASIS

Description

- ▶ An inflammatory process of the vagina, cervix, and vulva in women and lower genitourinary tract in man caused by a flagellate protozoan

Etiology

- ▶ The causative organism is *Trichomonas vaginalis*.
- ▶ Usually sexually transmitted; rarely transmitted by fomites
- ▶ Men can be asymptomatic carriers.

Incidence and Demographics

- ▶ Estimated 6 million women and partners infected annually

Risk Factors

- ▶ Risk factors listed under General Approach

Prevention and Screening

- ▶ Prevention listed in General Approach
- ▶ No routine screening
- ▶ Trichomoniasis screening should be conducted yearly for HIV-infected women

Assessment

History

- ▶ Incubation period is 4–20 days with an average of 1 week
- ▶ Women
 - ▶ May be asymptomatic
 - ▶ Severe pruritus; malodorous, profuse, gray-yellow or green vaginal discharge
 - ▶ Dysuria, dyspareunia, postcoital spotting, possible menorrhagia and dysmenorrhea
 - ▶ Onset of symptoms following menses
- ▶ Men
 - ▶ Usually asymptomatic
 - ▶ Dysuria, clear penile discharge, slight penile itching

Physical Exam

- ▶ Women
 - ▶ May have inguinal adenopathy
 - ▶ External genitalia may be irritated from scratching.
 - ▶ Vulva is erythematous and edematous.
 - ▶ Introitus, urethra, vagina, and cervix are coated with profuse malodorous, frothy, gray-yellow or green discharge.
 - ▶ Cervix or vagina has petechiae or strawberry patches appearance (characteristic).
- ▶ Men
 - ▶ Slight penile erythema with clear discharge

Diagnostic Studies

- ▶ Women
 - ▶ Saline wet mount of vaginal discharge to identify motile trichomonads
 - ▶ Vaginal pH > 4.5; Pap smear sometimes shows trichomonads
 - ▶ Potassium hydroxide (KOH) wet mount to rule out *Candida albicans*; positive whiff test (fishy odor) when KOH applied in BV
- ▶ Men
 - ▶ Microscopic exam of urine (first void in morning) positive for trichomonads

Differential Diagnosis

- ▶ Bacterial vaginosis
- ▶ Vulvovaginal candidiasis
- ▶ Gonorrhoea
- ▶ Pelvic inflammatory disease (PID)
- ▶ *Chlamydia trachomatis*

Management

Nonpharmacologic Treatment

- ▶ Concurrent treatment of sex partners
- ▶ Patients and sex partners should avoid sex until treatment completed and asymptomatic
- ▶ Screen for other STIs.
- ▶ Avoid alcohol with metronidazole (Flagyl) and for 72 hours after due to disulfiram-like reaction (severe nausea and vomiting).

Pharmacologic Treatment

- ▶ First treatment choice: Metronidazole (Flagyl) 2 g p.o. as single dose or tinidazole (Tindamax) 2 g p.o. as a single dose
- ▶ Alternative: Metronidazole (Flagyl) 500 mg p.o. b.i.d.

How Long to Treat

- ▶ Single dose or 7-day regimen; if regimen fails and patient remains symptomatic, re-treat with metronidazole (Flagyl) 500 mg p.o. b.i.d. for 7 more days or tinidazole (Tindamax) 2 g in a single dose. If there is frequent treatment failure, treat with metronidazole (Flagyl) 2 g p.o. daily for 3–5 days; consider culture for possible resistant strain of *T. vaginalis*.

Special Considerations

- ▶ Pregnancy: Metronidazole (Flagyl) 2 g p.o. in a single dose
- ▶ Allergy to metronidazole: There is no effective alternative. Clotrimazole (Lotrimin) may inhibit growth of *T. vaginalis* but does not eradicate it.

When to Consult, Refer, Hospitalize

- ▶ Consult on refractory cases not responding to treatment in 2 weeks.

Follow-up

- ▶ None indicated if asymptomatic following treatment
- ▶ Evaluate the patient's sex partner.

Expected Course

- ▶ Response prompt, although symptoms will return with re-infection

Complications

- ▶ Nausea or vomiting from oral metronidazole, disulfiram-like reaction from ingestion of alcohol and metronidazole, vulvovaginal candidiasis infection following 7-day treatment course
- ▶ Associated with preterm labor and premature rupture of membranes
- ▶ Pelvic inflammatory disease, bartholinitis, skenitis, cystitis

GONORRHEA**Description**

- ▶ A sexually transmitted bacterial infection caused by *Neisseria gonorrhoeae*

Etiology

- ▶ *Neisseria gonorrhoeae* is a Gram-negative diplococci present in exudate and secretions of infected mucous secretions occurring only in humans.
- ▶ Causes localized inflammatory conditions: Urethritis, epididymitis, proctitis, cervicitis, bartholinitis, pelvic inflammatory disease (salpingitis or endometritis), and pharyngitis in adults; vulvovaginitis in children; and conjunctivitis in newborns and adults; presence in children almost always a result of child sexual abuse
- ▶ Gonococcal bacteremia results in the disseminated systemic condition; arthritis-dermatitis syndrome sometimes associated with endocarditis or meningitis

Incidence and Demographics

- ▶ Transmission through intimate contact such as sexual intercourse; also parturition
- ▶ 60%–90% of women become infected following exposure.
- ▶ Greatest incidence in sexually active 15–29-year-olds
- ▶ Approximately 15% of infected women may develop PID with possible sterility if untreated.
- ▶ Most infections in men have symptoms that cause them to seek treatment before serious outcome. Many infected women do not have symptoms until complications are present.
- ▶ Common sites in women are the urethra, endocervix, upper genital tract, pharynx, and rectum.
- ▶ Common sites in men are the urethra, epididymis, prostate, rectum, and pharynx.

Risk Factors

- ▶ Risk factors listed under General Approach
- ▶ Homosexual males have 10× greater incidence.

Prevention and Screening

- ▶ Prevention methods listed under General Approach

- ▶ Yearly screening for sexually active and women ≤ 25 years if in an area of high GC prevalence
- ▶ Yearly screening for sexually active gay men, bisexual men, and men who have sex with men. Screen more frequently for men who have sex with multiple men or anonymous partners.
- ▶ Screen all pregnant women at initial prenatal visit and again early in third trimester.
- ▶ Prophylactic treatment to contacts of infectious patients

Assessment

History

- ▶ Incubation is short: Urethritis is 2–5 days, cervicitis is 5–10 days.
- ▶ Women: Often asymptomatic; dysuria, frequency, purulent urethral discharge, vaginal discharge, pelvic pain, spotting or abnormal menses; adolescent girls often have dissemination or progression within a week of menses
- ▶ Male: Could be asymptomatic; dysuria, urinary frequency, copious purulent (blood-tinged) penile discharge, testicular pain. Rectal symptoms: Erythematous, discharge, pain with defecation.
- ▶ Both may have conjunctivitis or pharyngitis as well.

Physical Exam

- ▶ Women: Purulent discharge from cervix, inflammation of Bartholin's glands; positive cervical motion tenderness (CMT) and signs of PID if untreated
- ▶ Men: Purulent urethral discharge, signs of prostatitis or epididymitis if untreated
- ▶ Disseminated gonorrhea: Stage 1, bacteremia with chills, fever, skin lesions (petechial or pustular skin rash); endocarditis or meningitis may occur; Stage 2, septic arthritis; knees, ankles, and wrists show erythema, edema, and pain.

Diagnostic Studies

- ▶ Cervical or urethral culture for *N. gonorrhoeae* using modified Thayer-Martin media
- ▶ Nucleic acid amplification test on first-void urine in men can be used in women but is less accurate
- ▶ DNA probe (can diagnose gonorrhea and chlamydia) for men and women

Differential Diagnosis

- | | |
|----------------------------|-------------------------------|
| ▶ PID | ▶ Nongonococcal pharyngitis |
| ▶ Nongonococcal cervicitis | ▶ <i>Chlamydia</i> infections |
| ▶ Urethritis | ▶ Arthritis |
| ▶ Proctitis | ▶ Vaginitis |

Management

Pharmacologic Treatment

- ▶ Uncomplicated gonococcal infections (genital, rectal and pharyngeal)
 - ▶ Ceftriaxone (Rocephin) 250 mg IM in a single dose *and* azithromycin 1 g orally in a single dose or doxycycline 100 mg orally twice daily for 7 days
 - ▶ If ceftriaxone is not available:
 - ▷ Cefixime 400 mg orally, plus either azithromycin 1 g orally or doxycycline 100 mg orally for 7 days is recommended
 - ▷ Azithromycin 2 g dose orally for severe allergy to cephalosporins
 - ▷ CDC recommends test of cure if alternative regimen is used.
- ▶ Mild to moderate PID treated as an outpatient: Ceftriaxone (Rocephin) 250 mg IM in a single dose plus doxycycline 100 mg p.o. b.i.d. for 14 days
- ▶ Gonococcal conjunctivitis: Lavage of infected eye with saline solution once, plus:
 - ▶ Ceftriaxone (Rocephin) 1 g IM × 1 dose
 - ▶ Neonates: 25–50 mg/kg IM or IV × 1 dose not to exceed 125 mg
 - ▶ Infants with gonococcal conjunctivitis: Ceftriaxone (Rocephin) 25–50 mg/kg IV or IM, not to exceed 125 mg in a single dose
 - ▶ Gonococcal infection in children who weigh > 45 kg: Treat the same as adults.
 - ▶ Gonococcal infection in children who weigh < 45 kg: Ceftriaxone 125 mg IM in a single dose

Special Considerations

- ▶ Pregnant women should be treated with a cephalosporin; erythromycin or amoxicillin can be used for presumptive or diagnosed *Chlamydia* infection.
- ▶ Pregnant and lactating women should not be treated with quinolones or tetracycline. If a pregnant woman cannot tolerate cephalosporins, treat with spectinomycin (Tobicin) 2 g IM × 1 dose alone (not currently available in the U.S.) with effective *Chlamydia* regimen.
- ▶ All infants born with neonatal ophthalmia should be observed for gonococcal sepsis and disseminated infection.

When to Consult, Refer, Hospitalize

- ▶ Hospitalize for disseminated gonorrhea.
- ▶ Hospitalize for severe PID.
- ▶ Refer patients unresponsive to treatment.

Follow-up

- ▶ Retest in 1–2 months following treatment if symptomatic.

Expected Course

- ▶ Usually there is prompt response to therapy.

Complications

- ▶ PID, sterility, salpingitis, epididymitis, prostatitis, disseminated gonococcal infection
- ▶ Perinatal postabortal endometritis and salpingitis, acute salpingitis, increased incidence of premature rupture of membranes, preterm delivery, chorioamnionitis, neonatal sepsis, postpartum sepsis, neonatal conjunctivitis
- ▶ May help facilitate HIV transmission

CHLAMYDIAL INFECTION

Description

- ▶ A sexually transmitted infection caused by *Chlamydia trachomatis*

Etiology

- ▶ *C. trachomatis* is an obligate intracellular parasite; transmission is by sexual or perinatal contact.
- ▶ Infection in women may ascend from cervicitis and urethritis to salpingitis and spread vertically to cause proctitis; in men, it may ascend the urogenital tract to epididymis and prostate.

Incidence and Demographics

- ▶ The most common sexually transmitted infection; prevalence is highest in persons age < 25.
- ▶ 4 million cases per year, prevalence 3–4 times greater than GC
- ▶ Leading cause of infertility, ectopic pregnancy, and PID; reportable to local health authority, case report required in most U.S. states.

Risk Factors

- ▶ Risk factors listed under General Approach
- ▶ Presence of concomitant STI, especially *N. gonorrhoeae*

Prevention and Screening

- ▶ Prevention methods listed under General Approach
- ▶ Annually screen sexually active men and women ≤ 25 years.
- ▶ When treating gonococcal infections, include treatment against possible co-infection with *C. trachomatis*.
- ▶ Screen pregnant women initially and repeat in the third trimester for high-risk women.

Assessment

History

- ▶ Incubation 6–14 days
- ▶ May be asymptomatic
- ▶ Women: Increase in mucopurulent vaginal discharge, low pelvic discomfort, dysuria, urinary frequency, spotting, and possibly dyspareunia; incubation period usually 1 week
- ▶ Men: Mucopurulent urethra discharge or dysuria

Physical Exam

- ▶ Cervix is friable, mucopurulent discharge; may have positive cervical motion tenderness, adnexal or uterine tenderness if untreated
- ▶ Occasional inguinal lymphadenopathy

Diagnostic Studies

- ▶ *Chlamydia* culture is definitive test but expensive
- ▶ DNA probe
- ▶ Nucleic acid amplification (PCR and LCR) in men on first-void urine; can also be used in women but less accurate

Differential Diagnosis

- ▶ PID
- ▶ Gonorrhea
- ▶ Salpingitis
- ▶ Urethritis

Management

Nonpharmacologic Treatment

- ▶ Sexual partners should be evaluated and treated.
- ▶ Patients should abstain from sexual intercourse until they and their sex partners have completed treatment: 7 days following single-dose treatment or after completion of a 7-day regimen.

Pharmacologic Treatment

- ▶ First choice: Azithromycin (Zithromax) 1 g p.o. single dose *or* doxycycline (Vibramycin) 100 mg p.o. b.i.d.
- ▶ Alternative choice: Erythromycin base 500 mg p.o. q.i.d. for 7 days *or* ofloxacin (Floxin) 300 mg p.o. b.i.d. *or* erythromycin ethylsuccinate 800 mg p.o. q.i.d.

How Long to Treat

- ▶ Single dose of azithromycin or 7-day course of treatment with all others

Special Considerations

- ▶ Neonatal ophthalmia and pneumonia may occur in infant born to infected mother; consult and treat with erythromycin IV.
- ▶ Doxycycline, ofloxacin, and erythromycin estolate contraindicated in pregnancy
- ▶ Ofloxacin contraindicated in patients < 17 years
- ▶ Pregnancy: Azithromycin 1 g p.o. in a single dose or amoxicillin 500 mg p.o. t.i.d.
- ▶ Children 6 months to 12 years with uncomplicated genital tract infection: Erythromycin 50 mg/kg/day divided q.i.d. × 7 days

When to Consult, Refer, Hospitalize

- ▶ Consult with physician for PID in pregnant women, recurrent infection, conjunctivitis, or neonatal infection.

Follow-up

- ▶ Not necessary if symptoms resolve with treatment with doxycycline, azithromycin, or ofloxacin
- ▶ If treated with erythromycin, reculture in about 3 weeks after initial treatment may be needed if symptoms persist or re-infection suspected
- ▶ Pregnant women need repeat cultures 3 weeks after therapy completion due to high noncompliance rate and lower efficacy of erythromycin regimens.

Expected Course

- ▶ Prompt resolution of symptoms
- ▶ May become re-infected if sexual partners are not treated

Complications

- ▶ PID, infertility, increased incidence of ectopic pregnancy; may help facilitate HIV transmission

MUCOPURULENT CERVICITIS

Description

- ▶ A sexually transmitted syndrome characterized by purulent discharge visualized on the cervix or in the endocervical canal, endocervical swab, or sustained endocervical bleeding easily induced by gentle passage of a cotton swab through the cervical os

Etiology

- ▶ May be caused by *C. trachomatis* and *N. gonorrhoeae*; 1/3 of cases, agent cannot be established
- ▶ Ureaplasma (related to *Mycoplasma hominis*) may be the responsible organism.

Incidence and Demographics

- ▶ Common in sexually active, especially young, women

Risk Factors

- ▶ Same as for *Chlamydia* and gonorrhea
- ▶ May be associated with frequent douching or exposure to chemical irritants

Prevention and Screening

- ▶ Prevention methods listed under General Approach
- ▶ Screening for *Chlamydia* and gonorrhea (see General Approach)

Assessment

History

- ▶ Often asymptomatic, abnormal vaginal discharge, vaginal bleeding postcoital

Physical Exam

- ▶ Cervix has purulent or mucopurulent exudate and is friable.

Diagnostic Studies

- ▶ DNA probe to test for gonorrhoea and *Chlamydia*
- ▶ Wet mount exam to test for *Trichomonas*
- ▶ A finding of leukorrhea (> 10 WBC/high power field) on wet mount has been associated with chlamydial and gonococcal infection of the cervix.
- ▶ Urine for culture and sensitivity

Differential Diagnosis

- ▶ *Gonorrhoeae* ▶ UTI
- ▶ *Trichomonas* ▶ *Chlamydia*
- ▶ PID

Management

Pharmacologic Treatment

- ▶ Treat according to suspicion for chlamydia, gonorrhea, or both. Wait for test results if prevalence of both organisms is low and chance for follow-up is good.
- ▶ See treatment for gonococcal and chlamydial infections.

How Long to Treat

- ▶ Treatment for chlamydia and gonorrhea single dose to 7 days per CDC guidelines

Special Considerations

- ▶ Treat pregnant women with cephalosporin, erythromycin, or amoxicillin, not with quinolones or tetracycline.

When to Consult, Refer, Hospitalize

- ▶ Consult for recurrent infection.

Follow-up

- ▶ Recommended for gonorrhea or chlamydia as appropriate
- ▶ If symptoms persist, patient should refrain from sexual activity and return for evaluation.
- ▶ Sexual partners should be examined and treated for STIs.

Expected Course

- ▶ Prompt response to treatment is expected.

Complications

- ▶ Depending on organism, same as for gonococcal or chlamydial infections

NONGONOCOCCAL URETHRITIS (NGU)

Description

- ▶ Inflammation of the urethra caused by a nongonorrheal infection characterized by mucopurulent or purulent discharge and burning

Etiology

- ▶ NGU if Gram-negative intracellular organisms are not identified on Gram stain
- ▶ *C. Trachomatis* is the major cause (23%–55%).
- ▶ Etiology of non-chlamydial NGU is unknown; however, *Ureaplasma urealyticum* and possible *Mycoplasma genitalium* may be present in as many as one third of cases
- ▶ Sometimes *Trichomonas vaginalis* and herpes simplex virus (HSV) cause NGU.

Incidence and Demographics

- ▶ Most common STI syndrome in males living in industrialized countries
- ▶ NGU more common than gonococcal urethritis in most areas of U.S.
- ▶ Proportion of NGU cases caused by *Chlamydia* has been declining gradually.

Risk Factors

- ▶ Risk factors listed under General Approach

Prevention and Screening

- ▶ Prevention methods listed under General Approach
- ▶ Screening for gonorrhea and chlamydia (see General Approach)

Assessment

History

- ▶ Patient reports urethral discharge that is purulent or mucopurulent, dysuria, urethral itching
- ▶ Recent unprotected sexual activity or new sex partner

Physical Exam

- ▶ Urethra erythematous and positive for purulent or mucopurulent discharge

Diagnostic Studies

- ▶ Gram stain of urethral secretions has ≥ 5 WBCs/oil immersion field without intracellular Gram-negative diplococci
- ▶ Positive leukocyte esterase test on first-void urine, or microscopic exam of first-void urine positive for > 10 WBCs/high power field
- ▶ DNA probe test for *N. gonorrhoeae* and *C. trachomatis*
- ▶ Nucleic acid amplification test for *Gonorrhoeae* and *Chlamydia* on urine sample

Differential Diagnosis

- ▶ Gonorrhea
- ▶ UTI
- ▶ Trichomoniasis

Management

Nonpharmacologic Treatment

- ▶ Sexual partners should be evaluated and treated appropriately.

Pharmacologic Treatment

- ▶ Defer treatment if no confirmation of urethritis, until results of DNA probe are back.
- ▶ Treat for *Chlamydia* (see Chlamydial Infection) as indicated.
- ▶ Empiric treatment of symptoms for high-risk patients if unlikely to return for follow-up.
- ▶ Empiric treatment covers infection with *Gonorrhoeae* and *Chlamydia* (refer to those entries).

How Long to Treat

- ▶ Treatment should be initiated immediately after diagnosis.
- ▶ A single dose is preferable due to better compliance; other regimens, treat for 7 days.

Special Considerations

- ▶ None

When to Consult, Refer, Hospitalize

- ▶ Refer for persistent or recurrent urethritis following adequate treatment.

Follow-up

- ▶ None necessary if resolves
- ▶ All sexual partners within the preceding 60 days should be referred for evaluation.

Expected Course

- ▶ Symptoms should be alleviated soon after treatment initiated.

Complications

- ▶ Epididymitis, prostatitis, Reiter syndrome, may help facilitate HIV transmission

PELVIC INFLAMMATORY DISEASE, CANDIDIASIS, BACTERIAL VAGINOSIS

See Chapter 11, Female Reproductive Disorders.

VIRAL INFECTIONS

GENITAL HERPES SIMPLEX VIRUS (HSV) INFECTION

Description

- ▶ Genital infection with primarily type 2 herpes simplex virus (HSV) and, less often, type 1 herpes simplex virus
- ▶ May present as a primary, latent, or recurrent disease
- ▶ No cure

Etiology

- ▶ HSV infection is transmitted through direct contact with mucous membranes and secretions.
- ▶ Primary infection causes local viral replication, seeding of regional neural ganglia, and possible viremia.
- ▶ Herpes viruses establish lifelong latency in neural ganglia and periodically reactivate.
- ▶ Up to 50% of first-episode cases of genital herpes are caused by HSV-1, but recurrences and subclinical shedding are much less frequent for genital HSV-1 infection than genital HSV-2 infection.
- ▶ Many HSV-2–infected people have not received a diagnosis of genital herpes and are unaware of transmission.

Incidence and Demographics

- ▶ 50 million people are infected with herpes in the United States.
- ▶ HSV is endemic in the U.S., with 776,000 new cases per year.
- ▶ 16.2% of people age 14–49 years have HSV infection.
- ▶ The highest frequency is in 15- to 29-year-olds.
- ▶ The incidence of primary or recurrent herpes is about 10% of pregnant women.
- ▶ Perinatal transmission occurs in 1:3,200 live births with 60% infant mortality.

Risk Factors

- ▶ Listed under General Approach

Prevention and Screening

- ▶ Prevention methods listed under General Approach; however, condoms may not block transmission of some lesions.
- ▶ Infected people should abstain from all sexual activity when lesions or prodromal symptoms are present.
- ▶ Sexual transmission of HSV can occur during asymptomatic periods. Asymptomatic viral shedding is more frequent in genital HSV-2 infection than genital HSV-1 infection and is most frequent during the first 12 months after acquiring HSV-2.
- ▶ Advise use of condoms during all sexual exposures; however, may not eliminate possibility of transmission
- ▶ Patients should be informed about the risks of neonatal infection.
- ▶ No routine screening

Assessment

History

- ▶ Genital lesions (occurring 2–14 days after exposure), which are painful papules followed by vesicles, ulceration, crusting, and healing
- ▶ First-episode symptoms consist of hyperesthesias, burning, itching, dysuria, pain, and tenderness in genital area; fever, myalgia, malaise, lymphadenopathy. Healing of initial lesions takes up to 21 days (average = 12 days).
- ▶ Recurrent episodes usually have prodrome (unusual sensation in area before eruption of lesions), recur in same region, and length of shedding is reduced (average 7 days). Healing occurs in approximately 5 days.

Physical Exam

- ▶ Examination of genital area for characteristic herpetic lesions: Tender vesicles on erythematous bases or ulcers in various stages of progression
- ▶ Enlarged lymph nodes in inguinal area

Diagnostic Studies

- ▶ Viral detection or culture from early lesion or vesicle is most sensitive and permits viral typing, which is helpful for prognostic information (HSV-1 has much lower risk for symptomatic recurrent outbreaks).

Differential Diagnosis

- ▶ Syphilis
- ▶ Chancroid
- ▶ *Molluscum contagiosum*
- ▶ Folliculitis
- ▶ Trauma, burn

Management

Nonpharmacologic Treatment

- ▶ Cool perineal compresses, sitz baths, loose-fitting clothes to help alleviate pain
- ▶ Good handwashing and hygiene to reduce autoinoculation to other body regions

Pharmacologic Treatment

- ▶ Topical acyclovir is less effective than oral; use is discouraged.
- ▶ First episode: Acyclovir (Zovirax) 400 mg p.o. b.i.d. *or* famciclovir (Famvir) 250 mg p.o. b.i.d. *or* valacyclovir (Valtrex) 1 g p.o. b.i.d. Treat 7–10 days.
- ▶ Recurrent infection: Acyclovir 400 mg p.o. t.i.d. × 5 days *or* acyclovir 800 mg p.o. b.i.d. × 5 days *or* acyclovir 800 mg p.o. t.i.d. × 2 days, *or* famciclovir 125 mg p.o. b.i.d. × 5 days *or* famciclovir 1,000 mg p.o. b.i.d. × 1 day
- ▶ Analgesics such as acetaminophen, NSAIDs, and topical astringents

How Long to Treat

- ▶ For first episode: 7–10 days or longer if lesions not completely healed
- ▶ For recurrent episode: 1–5 days
- ▶ Daily suppressive therapy; after 1 year of therapy, consider discontinuation to assess rate of recurrent episodes.
- ▶ For episodic recurrent infection, start treatment during prodrome or within 1 day after onset of lesions.

Special Considerations

- ▶ HIV+ or immunocompromised: Acyclovir 400–800 mg p.o. t.i.d. *or* famciclovir 500 mg p.o. b.i.d. *or* Valacyclovir 500 mg p.o. b.i.d. until clinically resolved; if severe, treat as for severe infection. If resistance suspected, consult with HIV specialist.
- ▶ All acyclovir-resistant strains are also resistant to valacyclovir; most are resistant to famciclovir.
- ▶ First clinical episode during pregnancy may be treated with acyclovir. Safety of acyclovir, valacyclovir, and famciclovir in pregnancy not established; benefits must outweigh risks.

- ▶ Prophylactic administration of acyclovir intrapartum for women with a history of HSV is not recommended.
- ▶ Cesarean delivery not always necessary with history of herpes, only recommended when active lesions visible at onset of labor
- ▶ Signs of congenital infection may occur from birth to 4–6 weeks (vesicles around eyes, mouth, skin; respiratory distress; central nervous system [CNS] infection; sepsis)

When to Consult, Refer, Hospitalize

- ▶ Consult if pregnant, serious infection, or infections resistant to treatment
- ▶ Hospitalize if suspected encephalitis, pneumonitis, or hepatitis, or congenital infection

Follow-up

Expected Course

- ▶ Most symptoms reduce promptly.
- ▶ Usually none indicated unless severe recurrent episodes and treatment inadequate

Complications

- ▶ Encephalitis, blindness, pneumonitis, hepatitis, perinatal transmission

HUMAN PAPILLOMAVIRUS INFECTION

Description

- ▶ Infection with certain subtypes of the human papillomavirus (HPV or genital warts) causing flat, papular, or pedunculated growths on the genital mucosa
- ▶ Visible warts are known as condyloma acuminata.

Etiology

- ▶ Virus enters body during sexual activity, via an epithelial defect, and infects stratified squamous epithelium of lower genital tract; visible genital warts are usually caused by HPV types 6 or 11
- ▶ HPV infection usually persists throughout patient's life in dormant state and becomes infectious intermittently; generally benign, may be asymptomatic or cause minor symptoms
- ▶ Highly contagious; 90%–100% of male partners of infected women become infected, mostly subclinically
- ▶ HPV infections with types 16, 18, and 31 strongly associated with cervical dysplasia
- ▶ HPV implicated in epithelial cancers, especially anorectal carcinoma, vulvar or penile cancer

Incidence and Demographics

- ▶ 79 million men and women are currently infected with HPV.
- ▶ 14 million men and women are infected annually.
- ▶ About 360,000 people are infected with genital warts yearly.
- ▶ More than 40 HPV types can infect the male and female genital area.
- ▶ Prevalent in females 14–59 years of age
- ▶ Most common viral STI in the U.S.

Risk Factors

- ▶ Risk factors listed under General Approach
- ▶ Early coitus and lack of barrier methods for contraception
- ▶ Growth of warts may be stimulated by oral contraceptives, pregnancy, or immunosuppression.

Prevention and Screening

- ▶ Prevention methods listed under General Approach; however, condoms may not eliminate risk of transmission entirely; patient with HPV still infectious even after warts removed
- ▶ Screening of women through annual Pap smear
- ▶ Gardasil, a quadrivalent vaccine against HPV types 6, 11, 16, and 18, recommended for males and females age 9–26
- ▶ Cervarix, a bivalent vaccine against HPV types 16 and 18, recommended for females ages 10–25; not recommended for males

Assessment

History

- ▶ Usually asymptomatic or can cause palpable lesion, itching, burning, local pain, or bleeding
- ▶ Significant lesions in some people
- ▶ May be unknown history of contact; incubation period from weeks to a year or longer

Physical Exam

- ▶ Small, flesh-colored, wart-like lesions; some can become confluent as one large wart
- ▶ Some warts flat or difficult to visualize, others are vegetative growths
- ▶ Women: Warts seen on labia, perianal areas, vagina, cervix, or mouth
- ▶ Men: Warts seen on shaft of penis, penile meatus, scrotum, perianal areas, and mouth

Diagnostic Studies

- ▶ Most warts are diagnosed by visualization. Applying 3%–5% acetic acid to the vulva of a woman or penis of a man to reveal white coloring of lesions (called acetowhitening).
- ▶ Pap smear on women detects koilocytosis, indicative of HPV.

- ▶ Should test for concomitant STIs: HIV, gonorrhea, syphilis, chlamydia
- ▶ Biopsy for detection of viral DNA available but not used clinically

Differential Diagnosis

- ▶ Condyloma latum
- ▶ Neoplasm
- ▶ Granuloma inguinale
- ▶ Moles
- ▶ Herpes simplex
- ▶ Syphilis
- ▶ Folliculitis
- ▶ Skin tags
- ▶ Keratosis
- ▶ Scabetic nodules

Management

Nonpharmacologic Treatment

- ▶ Smoking is a co-factor for cervical cancer with HPV; encourage cessation for woman infected with HPV.
- ▶ Examination of sexual partners is not recommended, since partner's role in re-infection is minimal.
- ▶ Encourage continued use of condoms.

Pharmacologic Treatment

- ▶ Drugs treat symptoms and may decrease size of wart; no treatment available that completely eradicates virus
- ▶ External/perianal warts
 - ▶ Patient-applied podofilox (Condylox) 0.5% solution or gel (apply b.i.d. × 3 days, then off 4 days); may repeat cycle total of 4 times *or*
 - ▶ Imiquimod (Aldara) 5% cream: Apply q.h.s. 3× week; wash off after 6–10 hours. May use up to 16 weeks, may clear in 8–10 weeks.
 - ▶ Provider-administered cryotherapy with liquid nitrogen, may repeat every 1–2 weeks
 - ▶ Provider-administered podophyllin (Podofin) 10%–25% in compound tincture of benzoin (wash off thoroughly 1–4 hours after application); repeat weekly if necessary *or*
 - ▶ Provider-administered trichloroacetic acid (TCA) 80%–90%; apply only to warts. Powder with talc or baking soda to remove acid. Repeat weekly if necessary.

How Long to Treat

- ▶ Depending on the size of wart and response to treatment, could take one to several treatments

Special Considerations

- ▶ Pregnancy: Podophyllin, imiquimod, podofilox are contraindicated.
- ▶ Some specialists recommend removal of visible warts during pregnancy.
- ▶ HIV patients may not respond well to treatment.

When to Consult, Refer, Hospitalize

- ▶ Vaginal and cervical warts: Consult with gynecologist; dysplasia must be excluded before treatment instituted.
- ▶ Warts on rectal mucosa should be referred to proctologist.
- ▶ Refer women with large warts (> 2 cm) to gynecologist for treatment with CO₂ laser, electrodesiccation, electrocautery, cryocautery, or LEEP (loop electrosurgical excision procedure [gynecologic surgery]).

Follow-up

- ▶ During therapy, women should continue to have regular, annual Pap smears.

Expected Course

- ▶ Treatment of warts may require several visits for provider-administered treatment.
- ▶ Genital warts can resolve on their own, remain unchanged, or continue to grow untreated.
- ▶ Reoccurrence of warts is common, especially within the first 3 months following treatment.

Complications

- ▶ Cervical dysplasia and cervical squamous cell carcinoma; invasive carcinoma of vulva and penis
- ▶ Anal squamous cell carcinoma of bisexual or homosexual males
- ▶ Scarring from treatment procedures

OTHER SEXUALLY TRANSMITTED INFECTIONS

SYPHILIS

Description

- ▶ Sexually transmitted disease affecting many organs throughout body, caused by *Treponema pallidum*
- ▶ Clinical stages include primary, secondary, early latent (up to 1 year duration), late latent, tertiary

Etiology

- ▶ *T. pallidum*: Spirochete that invades the human body by penetrating intact skin or mucous membrane during sexual contact
- ▶ Once inside body, rapidly multiplies and spreads to regional lymph nodes
- ▶ Congenital: Occurs from transplacental passage of organism occurring any time during gestation; can result in spontaneous abortion (second trimester), stillbirth

Incidence and Demographics

- ▶ Increase in cases of syphilis in men who have sex with men (MSM)
- ▶ In 2008, 63% of reported primary and secondary syphilis cases were among MSMs.
- ▶ Rates of primary and secondary syphilis increased in men and women age 15–24 in 2007.
- ▶ Approximately 55,400 new cases are reported in the U.S. annually.
- ▶ The congenital syphilis rate has decreased in recent years.

Risk Factors

- ▶ Listed under General Approach

Prevention and Screening

- ▶ Prevention methods listed under General Approach
- ▶ Early diagnosis and treatment with partner notification and treatment
- ▶ Routine screening for persons ≤ 25 years in high-prevalence areas; also screen patients with other STIs
- ▶ Pregnancy: Screening at first prenatal visit, then repeat for high-risk population at 28 weeks and delivery

Assessment

History and Physical Exam

- ▶ See Table 13–1.

TABLE 13-1
STAGES OF ACQUIRED SYPHILIS

PRIMARY	SECONDARY	LATENT	TERTIARY
Painless ulcer or chancre at site of inoculation 3–4 weeks after exposure Extragenital lesions such as lips or breast may be painful Primary chancre is highly infectious, heals spontaneously after 1–5 weeks and patient may not seek treatment	Rash is macular, papular, annular, or follicular (rarely pustular) and often present on palms and soles In warm, moist areas, may develop broad flat lesions (condylomata lata) Rash lasts 2–6 weeks, then heals spontaneously Mucous patches appear as gray erosions noted in mouth, throat, on cervix Generalized lymphadenopathy Arthralgias, myalgias, and “flu-like” symptoms	Begins with healing of the lesions in secondary stage Early latent < 1 year (infectious) Late latent > 1 year (noninfectious) Sometimes difficult to distinguish early latent from late latent stage due to unknown duration of symptoms Meningitis Cardiovascular disease, arthritis, neurologic lesions Often asymptomatic	Gummatous formation, cardiovascular or neurosyphilis

- ▶ Primary
 - ▶ Incubation is approximately 3 weeks and ranges 10–90 days after exposure.
 - ▶ Painless, indurated ulcer (chancre) at site of inoculation is highly infectious, heals spontaneously after 1–5 weeks and patient may not seek treatment; may be regional lymphadenopathy
 - ▶ Extragenital (lips, breast) lesions may be painful.
- ▶ Secondary
 - ▶ May occur from 6 weeks to 6 months after primary stage; most contagious
 - ▶ Rash is macular, papular, annular, or follicular and often present on palms and soles.
 - ▶ Rash lasts 2–6 weeks, then heals spontaneously.
 - ▶ Moist, raised lesions of the skin (condyloma lata) and mucous patches in mouth and throat, on cervix
 - ▶ Generalized lymphadenopathy
 - ▶ Arthralgias, myalgias, and “flu-like” symptoms
- ▶ Latent
 - ▶ Asymptomatic, begins with the end of secondary symptoms
 - ▶ Early latent < 1 year (infectious)
 - ▶ Late latent > 1 year (noninfectious)
 - ▶ Difficult to distinguish early latent from late latent stage if unknown duration of symptoms
- ▶ Tertiary
 - ▶ Gummatous formation, cardiovascular or neurosyphilis
- ▶ Congenital: Asymptomatic until age 2; failure to thrive, skin rash, jaundice, rhinitis, hepatosplenomegaly

Diagnostic Studies

- ▶ Definitive method: Darkfield microscopy and direct fluorescent antibody tests of lesion exudate or tissue
- ▶ Serologic tests: RPR, VDRL for initial testing and titers, FTA-ABS, MHA-TP to confirm diagnosis in people with positive RPR or VDRL
- ▶ For sequential serologic tests, use the same test (VDRL or RPR); titer will decrease with time and treatment.
- ▶ Four-fold increase in titer indicates new infection.
- ▶ Failure to achieve four-fold decrease in titer in 1 year indicates failed treatment.
- ▶ Latent syphilis of > 1 year duration, cardiovascular syphilis, and neurosyphilis: Serologic tests and lumbar puncture with tests on cerebrospinal fluid (CSF)
- ▶ Test for other STIs: HIV, gonorrhea, chlamydia.

Differential Diagnosis

- ▶ Genital ulcers
- ▶ Genital herpes
- ▶ Chancroid
- ▶ Neoplasm
- ▶ Lymphogranuloma venereum
- ▶ Superficial fungal infections

Management

Nonpharmacologic Treatment

- ▶ Abstain from sexual activity until treatment is complete.
- ▶ Early infection (primary, secondary, and early latent) and congenital syphilis reportable in all U.S. states

Pharmacologic Treatment

- ▶ Patients exposed sexually to a patient who has syphilis in any stage should be evaluated clinically and serologically and treated in the following cases:
 - ▶ People exposed within 90 days preceding diagnosis of primary, secondary, or early latent stages in a sex partner, even if seronegative
 - ▶ People exposed > 90 days before the diagnosis of primary, secondary, or latent stages in a sex partner and in whom serologic test results are not available immediately and the opportunity for follow-up is uncertain
 - ▶ For purposes of partner notification and presumptive treatment of exposed sex partners, patients with unknown duration of illness and high serologic test titers ($\geq 1:32$) may be considered as having early syphilis.
- ▶ Patients with symptoms or history of symptoms and positive diagnostic studies, see Table 13-2

TABLE 13-2
RECOMMENDED TREATMENT OF ACQUIRED SYPHILIS

STAGE OF DISEASE	TREATMENT REGIMEN
Primary, secondary, and early latent disease	Benzathine penicillin G 2.4 million units IM in single dose Penicillin-allergic patients: Doxycycline 100 mg b.i.d. \times 28 days, or tetracycline 500 mg orally q.i.d. \times 28 days
Late latent syphilis or syphilis of unknown duration	Benzathine penicillin G 2.4 million units IM \times 3 each at 1-week intervals Penicillin-allergic patients: Doxycycline 100 mg orally b.i.d. for 4 wks, or tetracycline 500 mg orally q.i.d. \times 4 wks
Tertiary disease, excluding neurosyphilis	As for late latent disease, with appropriate management of complications
Neurosyphilis	Aqueous cystamine penicillin G, 18-24 million units/day given as 3-4 million units IV every 4 hours for 10-14 days, or procaine penicillin 2-4 million units IM a day <i>plus</i> probenecid (Benemid) 500 mg orally q.i.d., both for 10-14 days

Special Considerations

- ▶ HIV-infected people
 - ▶ Serologic tests and interpretation the same as for HIV-infected patients
 - ▶ When clinical finding suggests syphilis, but serologic tested nonreactive or unclear, use alternative test such as biopsy of lesion, darkfield examination, or direct fluorescent antibody staining of lesion material.
 - ▶ Treatment the same as for HIV-negative people
 - ▶ Neurosyphilis must be considered in differential for HIV+ patients. CSF examination should be performed on HIV-infected people who show mental status changes or have either late latent syphilis or syphilis of unknown duration.
 - ▶ Penicillin must be used to treat; if penicillin-allergic, must be desensitized
 - ▶ Primary and secondary syphilis should have VDRL/RPR serology at 3, 6, 9, 12, and 24 months to evaluate for treatment failure. If titer increased four-fold, fails to decrease four-fold at 3 months, or symptoms persist, retreatment is indicated.
- ▶ Pregnancy: Treat for appropriate stage of syphilis.
 - ▶ Some experts recommend a second dose of benzathine penicillin 2.4 mil units IM 1 week after initial dose for pregnant women with primary, secondary, or early latent syphilis. If penicillin-allergic, desensitize patient to penicillin.
 - ▶ Women treated in second trimester are at risk for premature labor and fetal distress.
- ▶ Infants born to mothers with positive nontreponemal and treponemal test
 - ▶ If infant was born to mother who tests positive for syphilis but adequate treatment with penicillin is not documented, the infant should be observed for congenital syphilis (into early childhood).
 - ▶ Routine physical exams for rash, hepatomegaly, lymphadenopathy, persistent rhinitis
 - ▶ Quantitative nontreponemal test on infant's blood (not cord blood)
 - ▶ Cerebrospinal fluid testing, long bone X-rays, and other testing may be indicated.
- ▶ All patients may experience the Jarisch-Herxheimer reaction.
 - ▶ Upon treatment of primary or secondary syphilis, occurs due to lysis of treponemes
 - ▶ Experience fever, chills, headache, myalgias, rash
 - ▶ Treated with antihistamines and antipyretics

When to Consult, Refer, Hospitalize

- ▶ Consult with physician or refer to infectious disease specialist for pregnant women, congenital syphilis, neurosyphilis infection, or HIV+ patients.
- ▶ Hospitalize for parenteral therapy and for penicillin desensitization therapy.

Follow-up

- ▶ Primary and secondary syphilis: Examine clinically and serologically at 6 or 12 months or more frequently if clinically indicated; if serologic titer (VDRL or RPR) has not declined by four-fold in 6 months after therapy, consider treatment a failure.

- ▶ Treatment failure: Reevaluate for HIV infection, provide more frequent follow-up (3 months instead of 6). If additional follow-up cannot be ensured, retreatment recommended (3 weekly IM injections of penicillin G 2.4 million units).
- ▶ Consider CSF examination.
- ▶ Latent syphilis: Serologic testing at 6, 12, and 24 months; evaluate for neurosyphilis and re-treat if titers increase four-fold, initial high titer (> 1:32) fails to decline at least four-fold within 12–24 months, or symptomatic

Expected Course

- ▶ Primary stage lasts 1–5 weeks, secondary stage lasts 2–6 weeks.

Complications

- ▶ Tertiary syphilis: Cardiovascular involvement causing aortitis, aortic insufficiency, aneurysm, and neurosyphilis; recurrent secondary symptoms possible within 1 year for 25% cases.

CASE STUDIES

CASE 1. A 23-year-old sexually active male presents with a 4–5 day history of dysuria he feels is caused by a urinary tract infection.

HPI: Denies frequency, fever, flank pain, hematuria, history of urinary tract infections.

- ▶ What additional information will help you evaluate this patient?

Exam: Mucopurulent urethral discharge, no inguinal adenopathy, no genital lesions.

- ▶ What is the differential diagnosis?
- ▶ Should any diagnostic tests be done?
- ▶ What are your treatment considerations?

CASE 2. A 17-year-old female comes to the family planning clinic for routine pelvic exam and contraception. She has had 4 sexual partners in the past year and only occasionally uses condoms. She requests an HIV test because one of her recent partners is an IV drug user.

PMH: History of 2 pregnancies with 2 abortions, no major illnesses, does not smoke, drinks 2–3 beers on the weekend, lives with mother and grandmother, in 11th grade, failing some classes.

- ▶ What additional information should you obtain?

Exam: Complete physical exam with no significant findings except flat-topped, fleshy-colored lesions on labia minora and thin yellow vaginal discharge.

- ▶ What screening tests should be done?
- ▶ What treatment should be considered today?
- ▶ What education and prevention topics should be discussed with this patient?

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