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Sexually Transmitted Diseases (STDs)

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18 Sexually transmitted diseases (STDs)

Donald E. Greydanus, Jane Seyler, and Hatim A. Omar

High rates of unprotected sexual behavior in adolescents result in millions of cases of STDs in the world. This chapter reviews factors inducing high STD rates, specific STDs, and their management based on 2010 U.S. Centers for Disease Control and Prevention (CDC) STD guidelines. Clinicians should screen all their sexually active adolescent patients for STDs and provide preventive education as well as treatment measures.

18.1 Introduction

There are many STDs, which can infect adolescents (see ►Tab. 18.1) (1,2,3,4,5). Sexually active adolescents are at risk for STDs due to their high rates of sexual activity, multiple sex partners, immature cervix (cervical ectropion, which is a good media for growth of some STD agents), other high risk behaviors that encourage sexual behavior (i.e. substance abuse, body piercing, tattoos), mistrust of adults in general, problems traversing the medical system, and an often pervasive belief (“magical thinking”) that they are not susceptible to acquiring STDs. The growth of social networks in the past 20 years has led to another risk factor for allowing youth to meet and acquire STDs. Adolescents receive limited sexual education in the United States, have accidental or irregular sexual relationships, change sexual partners (“serial monogamy”), and fail to use condoms on a regular basis.

The result is that 19 million STDs are acquired in the United States each year, mainly in the 14- to 29-year-old age group; one in six sexually active adolescents (15 to 19 years of age) acquire an STD each year, and one in three persons acquire an STD by age 24 years. Those at the highest risk for an STD include runaway youth, those involved in survival sex (prostitution), those in jails or detention centers, those involved in male homosexual activity, and youth with a history of STDs. The most common STDs among youth are infections due to HPV (6,7,8,9), HSV (10,11), *C. trachomatis* (12,13), *N. gonorrhoeae* (14), and *T. vaginalis* (15,16,17,18,19). The highest rates of chlamydial and gonococcal infections are in 15- to 19-year-old females, while HPV acquisition is often during adolescence. Oral sexual behavior is noted in one-third to one-half of youth and can lead to the acquisition of various STDs including HPV, HSV, syphilis, gonorrhea, and others. Clinicians should note that *N. gonorrhoeae* is part of the differential diagnosis of pharyngitis in adolescents (see ►Tab. 18.2), and thus questions about oral sexual behavior are important even when sore throat is the only presentation.

Primary prevention of STDs involves proper counseling of youth regarding STDs (including HIV), use of latex condoms for all sexually active youth, and immunization with HPV, hepatitis A, as well as hepatitis B vaccines (including for males having sex with men and illicit drug users). Use of a condom is a marker for improved risk behavior in adolescents and is beneficial in lowering STD rates, especially with

Tab. 18.1: STD agents (diseases or infections; STDs or sexually transmitted infections [STIs]).

Human papillomavirus (HPV)	Hepatitis A, B, C
<i>Trichomonas vaginalis</i>	<i>Haemophilus ducreyi</i> (chancroid)
<i>Chlamydia trachomatis</i>	Pediculosis pubis
<i>Neisseria gonorrhoeae</i>	<i>Sarcoptes scabiei</i> (scabies)
Herpes simplex virus (HSV)	<i>Gardnerella vaginalis</i> (bacterial vaginosis, or BV) (sexually associated)
Human immunodeficiency virus (HIV)	<i>Klebsiella granulomatis</i> (lymphogranuloma venereum, or LGV)
<i>Treponema pallidum</i> (syphilis)	Behcet's disease
<i>Molloscum contagiosum</i>	Reiter's syndrome
<i>Donovania granulomatis</i> (<i>Granuloma inguinale</i>)	Others

Tab. 18.2: Differential diagnosis of exudative, diffuse, or membranous pharyngitis.

Cause	Description	Treatment
Group A β - hemolytic streptococcus	Exudative, diffuse, or membranous type. Other features: strawberry tongue, tender anterior cervical lymphadenopathy, fever, leukocytosis, dysphagia, and headache. Minimal coryza and cough. Positive throat culture. Scarlet fever can occur. Can occur with infectious mononucleosis.	1.2 million U benzathine penicillin intramuscularly (IM) or oral penicillin, 250 mg, qid $\times$ 10 days; erythromycin, 250 mg, qid $\times$ 10 days; Cefaclor: 250 mg qid $\times$ 10 days; others.
Infectious mononucleosis (Epstein-Barr virus)	Exudative, diffuse, or membranous erythema. Periodic fever, lymphadenopathy (especially anterior cervical), splenomegaly, absolute lymphocytosis, positive heterophil agglutination test (or other serologic evidence of infectious mononucleosis).	Supportive
Gonococcal pharyngitis (<i>N. gonorrhoeae</i>)	Exudative pharyngitis or diffuse erythema of the oropharynx associated with anterior cervical lymphadenopathy and history of oral sex with an	Ceftriaxone 250 mg IM + treatment for <i>C. trachomatis</i> : see box "Treatment of <i>C. trachomatis</i> Cervicitis (Urethritis)"

(Continued)

Tab. 18.2: Differential diagnosis of exudative, diffuse, or membranous pharyngitis. (Continued)

Cause	Description	Treatment
Adenovirus pharyngitis	infected sexual partner. Often asymptomatic. Pharynx may be the only site of infection in 1%–4% of teenagers with gonorrhea. Common cause of nonstreptococcal exudative pharyngitis and nasopharyngitis and follicular pharyngitis; diffuse erythema also noted, with fever, coryza, and cough.	Supportive
Acute lymphonodular pharyngitis (coxsackievirus A ₁₀)	Raised, white or yellow lesions with surrounding erythema on the posterior pharynx.	Supportive
Herpangina (coxsackievirus A)	Papulovesicular lesions leading to ulcerations occur on the pharynx. Presents as a febrile illness – often in the summer. Echovirus and enterovirus also implicated.	Supportive
Hand, foot, and mouth disease (coxsackievirus A ₁₆)	Vesicular and ulcerative lesions in the mouth and pharynx with vesicular eruptions over hands and feet.	Supportive
Postanginal sepsis (<i>Fusobacterium necrophorum</i> and <i>Bacteroides</i> species)	Evidence of pharyngeal infection followed by high fever, chills, anterior cervicitis, multiple abscesses, jaundice, etc.	Caused by anaerobic bacteria. Treatment involves antibiotics – depending on culture results – penicillin, clindamycin, metronidazole, etc.
<i>Corynebacterium haemolyticum</i>	Variable pharyngitis associated with a scarlatiniform eruption of arms and legs with eventual scaling of hands and feet in some. Urticarial rash and erythema nodosum noted in some.	Erythromycin, 250 mg, qid x 10 days. Penicillin not reliable.

qid, four times daily.

N. gonorrhoeae, *C. trachomatis*, and HIV. Spermicides with nonoxynol-9 are not recommended at this time because of their failure to prevent various STDs and potential injury to the surface of epithelial cells linked with its use that may enhance the acquisition of HIV.

Secondary prevention of STDs involves regular STD screening of all sexually active youth, evaluation for STDs, proper treatment of identified STDs (including

asymptomatic infection), and partner notification in the presence of STDs. Screening sexually active teenagers and adults includes annual testing for *C. trachomatis* (up to age 25 years); annual testing for *N. gonorrhoeae*, if at risk; and annual HIV screening, if sexually active as well as using injection drugs. Self-collection vaginal swabs for *C. trachomatis* and *N. gonorrhoeae* are becoming increasingly acceptable to adolescent females. One should consult with the CDC 2010 STD guidelines for STD management including STDs in special circumstances, such as STDs in pregnancy, males having sex with men (MSM), STDs in children, women having sex with women, those in correctional institutions, and others.

18.2 *C. trachomatis*

Two species of *Chlamydia* are recognized: *Chlamydia psittaci* (causing psittacosis) and *C. trachomatis*. The latter consists of different subspecies, which can cause cervicitis, urethritis, trachoma, and/or lymphogranuloma venereum. *C. trachomatis* is an obligate intracellular microbe, which causes the most commonly reported bacterial STD in the United States and, as noted with STDs, is disproportionately increased in minority adolescent females. It causes cell damage with a significant inflammatory host cell immune response. Two to three million infections are estimated to occur each year in the United States, and the prevalence in 18 to 26 year olds is nearly 5 percent in females and nearly 4 percent in males.

C. trachomatis is a bacteria that can cause a variety of infections (see the following box) that include cervicitis, urethritis (with dysuria, urethral discharge [often thin]), epididymitis, proctitis, pharyngitis, proctitis, perihepatitis (Fitz-Hugh-Curtis syndrome), and endocervicitis (pelvic inflammatory disease, or PID) (12,13). All sexually active females under age 25 years should be screened annually for the presence of this bacteria, which can be silent (asymptomatic) in half or more of those infected. A variety of diagnostic tests are available, as noted in ►Tab. 18.3. Nucleic acid amplification testing (NAAT) and DNA probes can be done on vaginal or cervical material as well as urine. NAAT sensitivity is excellent, in the range of 87 percent to 97 percent.

Tab. 18.3: Diagnostic tests for *C. trachomatis*.

Cell culture ("gold standard")
Polymerase chain reaction (PCR) test (NAAT)
Ligase chain reaction test (NAAT)
Enzyme-linked immunoassay (EIA, ELISA)
Direct fluorescent antibody (DFA)
DNA probes (Gen-Probe; direct hybridization probe test)
LET (leukocyte esterase dipstick)

***C. trachomatis* Infections**

1. Cervicitis
2. Urethritis
3. Salpingitis
4. Peritonitis
5. Perihepatitis (Fitz-Hugh-Curtis syndrome)
6. Urethral syndrome (dysuria/urethral syndrome)
7. Epididymitis
8. Conjunctivitis
9. Pharyngitis
10. Otitis media
11. Pneumonia
12. Endocarditis
13. Prostatitis
14. Proctitis (LGV stain)
15. ? Arthritis
16. Reiter's syndrome
17. Others

18.3 Cervicitis

This can present in various ways, though there typically is purulent or mucopurulent cervical discharge, erythema of the vaginal erythema, and hypertrophic cervical erosion. Mixed infections with other STDs are common, especially *N. gonorrhoeae*. Treatment of cervicitis due to *C. trachomatis* is outlined in the following box. When diagnosis cannot be confirmed, treatment for *N. gonorrhoeae* should be included due to the high incidence of coinfections. Azithromycin is effective for chlamydial infections in pregnancy.

Treatment of *C. trachomatis* cervicitis (urethritis)

1. Azithromycin, 1 g, orally as one dose or
2. Doxycycline, 100 mg, orally, twice a day for 7 days or
3. Alternative: Ofloxacin, 300 mg, orally, twice a day for 7 days or
4. Alternative: Erythromycin base, 500 mg orally, four times a day for 7 days or
5. Alternative: Erythromycin ethylsuccinate, 800 mg, orally, four times a day for 7 days or
6. Alternative: Levofloxacin, 500 mg, orally, once a day for 7 days

18.4 Urethritis and epididymitis

Urethritis due to *C. trachomatis* is usually present with dysuria and a thin or nonpurulent urethral discharge; mucopurulent or purulent discharge may also be seen. It may be present with other STD agents including *N. gonorrhoeae*, *Ureaplasma urealyticum*, or *T. vaginalis*. Urethritis due to *C. trachomatis* and *U. urealyticum* have the same clinical appearance and both usually respond to doxycycline or erythromycin. Male urethritis may also be due to *Mycoplasma genitalium* or HSV.

A first-void urine evaluation may reveal the presence of *T. vaginalis* in those with nongonococcal urethritis (NGU). Dysuria associated with pyuria can be due to *C. trachomatis* (urethral syndrome). Pharyngitis is uncommon and usually due to *N. gonorrhoeae* or HSV. Caucasian males with HLA-B27 who develop chlamydial urogenital infection may subsequently develop Reiter's syndrome. PID, ectopic pregnancy, and infertility may occur.

The recommended treatment schedule for uncomplicated chlamydia urethritis is azithromycin (1 gram orally in a single dose) or doxycycline (100 mg twice a day orally for 7 days) (see the previous box, "Treatment of *C. trachomatis* Cervicitis"). Azithromycin is preferred for those who may be nonadherent due to its single dosing regimen, while erythromycin may lead to nonadherence due to gastrointestinal intolerance. Alternative treatments include erythromycin base (500 mg orally four times a day for 7 days), erythromycin ethylsuccinate (800 mg orally, four times a day for 7 days), ofloxacin (300 mg orally twice a day for 7 days), or levofloxacin (500 mg orally for 7 days). Doxycycline, ofloxacin, and levofloxacin are contraindicated in pregnancy. Recommended regimens for the pregnant patient include azithromycin (1 gram orally) or amoxicillin – 500 mg orally three times a day 7 days. Alternatives for the pregnant patient include erythromycin base (not estolate) – 500 mg four times a day orally for 7 days or 250 mg orally, four times a day for 14 days; also, erythromycin ethylsuccinate (400 mg, orally four times a day for 14 days or 800 mg four times a day for 7 days) can be used. Erythromycin estolate is contraindicated in pregnancy due to drug-induced hepatotoxicity. Follow-up evaluation is necessary, as is treatment of sexual contacts.

Treatment of recurrent and persistent urethritis with other regimens (if there was compliance with the regimens already noted and reexposure did not occur) includes metronidazole (2 grams orally in a single dose) or tinidazole (2 grams orally in a single dose) *plus* azithromycin (1 gram orally) if not used already. *M. genitalium* is best treated with azithromycin. Epididymitis due to *C. trachomatis* or *N. gonorrhoeae* is treated with ceftriaxone (250 mg IM in a single dose for the gonorrhea) *plus* doxycycline (100 mg orally twice daily [BID] for 10 days); alternative regimens, if the infection is due to enteric organisms, include ofloxacin (300 mg orally BID for 10 days) or levofloxacin (500 mg orally once daily for 10 days) (1). For males at risk for both types of pathogens, ceftriaxone *plus* a fluoroquinolone is recommended.

18.5 *N. gonorrhoeae*

There are an estimated 1 million cases of gonorrhea in the United States each year, and at least 25 percent of cases occur in the 10- to 19-year-old age group. *N. gonorrhoeae*

is a bacteria (gram-negative diplococcus) that can produce urethritis, cervicitis, epididymitis, proctitis, conjunctivitis (neonatal ophthalmia), pharyngitis, perihepatitis, endocervicitis (PID), disseminated gonococcal infection (DGI with dermatitis and arthritis), and others (14). Classically, this organism produces a vaginitis in prepubertal girls and a cervicitis (with or without salpingitis) in pubescent girls and adult women. Gonorrhea has a tendency to infect the columnar epithelium of the cervical canal and the urethra, producing a carrier state that can last for months to years. This organism of antiquity possesses a genetic-based proclivity to alter antigenic structures on surfaces.

After an incubation period of 2 to 6 days, the symptomatology is protean, but usually there is a yellowish-green, mucopurulent endocervical discharge associated with minimal pruritus and with possible tenderness noted on cervical motion; the dysuria can be severe. Purulent endocervical discharge is a hallmark of gonorrhea, but this can be noted with trichomoniasis, chlamydial infection, and HSV infection. Abnormal uterine bleeding and urinary tract infection symptoms are also typical of gonorrhea. It can also cause a urethritis, dysuria/urethral discharge syndrome, salpingitis, proctitis, pharyngitis, conjunctivitis, and DGI in females. In males, it may lead to urethritis, epididymitis, proctitis, pharyngitis, conjunctivitis or DGI.

Urethritis is defined by classic symptoms (dysuria, urethral discharge) along with finding five or more polymorphonuclear leukocytes (PMNs)/1,000X magnification versus cervicitis with more than 30 PMNs/1,000X magnification. A Gram stain of the discharge reveals pairs of gram-negative, kidney-bean-shaped diplococci in the PMNs; this test is diagnostic in males but has decreased sensitivity in females. Other confirmatory laboratory testing includes culture on selective medium (Thayer-Martin medium in a 10 percent carbon dioxide environment), urinary PCR (NAAT) testing, or DNA hybridization testing (i.e. Gen-Probe). Approximately 50 percent of NGU have no defined organism; identified etiologic agents include *C. trachomatis*, *M. genitalium*, adenoviruses, HSV, and others (20). NGU typically has an incubation period of 2 to 3 weeks, an insidious onset, and intermittent dysuria as well as variable discharge.

Management of uncomplicated gonococcal infections of the cervix, urethra, or rectum is noted in ►Tab. 18.4. Screen adolescents with *N. gonorrhoeae* for *C. trachomatis*, *T. pallidum*, and HIV. Treatment should also include coverage for *C. trachomatis* since it is present in up to 40 percent of cases (►Tab. 18.3). Unfortunately, antibiotic resistance, a phenomenon begun in the twentieth century, is worsening in the twenty-first century; this includes resistance to penicillin, tetracycline, spectinomycin, quinolones, and floxacins. Other cause of male urethritis are noted above under *C. trachomatis*. Treatment of uncomplicated gonococcal infection of the pharynx is with ceftriazone (250 mg IM) plus azithromycin (1 gram orally) or doxycycline (100 mg twice a day for 7 days).

18.6 PID

PID is a polymicrobial infection of female genital tract that can include *C. trachomatis* and *N. gonorrhoeae*, this polymicrobial infection may involve such agents found in the vagino-cervical endogenous flora – such as *G. vaginalis*, beta-hemolytic streptococcus,

Neisseria meningitidis, *M. genitalium*, *Bacteroides fragilis*, *Streptococcus faecalis*, *U. urealyticum*, *Haemophilus influenzae*, coliforms (enterobacteriaceae), cytomegalovirus, peptostreptococcus, and other anaerobes (21,22). Screening for and management of *C. trachomatis* can help to prevent PID. ►Tab. 18.5 notes CDC criteria for PID that revolve around lower genital tract inflammation with pelvic organ tenderness. The following box, “Differential Diagnosis of PID,” notes the differential diagnosis for PID; if PID is clinically severe, consider hospitalization and imaging to look for tubo-ovarian abscess.

Tab. 18.4: Antibiotic management of gonococcal infections of the cervix, urethra, or rectum (uncomplicated) (1).

-
1. Ceftriaxone, 250 mg IM, one dose, or (if not an option)
 2. Cefixime, 400 mg, orally, one dose, or
 3. Single-dose injectable cephalosporin regimens
 - a. Ceftizoxime 500 mg IM
 - b. Cefotaxime 500 mg IM
 - c. Cefoxitin 2 grams IM + probenecid (1 gram orally)

Plus

Azithromycin (1 gram orally in one dose) *or*
 Doxycycline (100 mg orally twice a day, 7 days)

Tab. 18.5: Diagnostic criteria for PID (1).

-
1. Minimal criteria
 - a. Uterine tenderness, or
 - b. Adnexal tenderness, or
 - c. Tenderness on cervical motion
 2. Additional criteria
 - a. Cervical (vaginal) mucopurulent discharge
 - b. Oral temperature over 101 degrees F (over 38.3 degrees C)
 - c. Examination of saline drop from discharge: see white blood cells
 - d. Elevated C-reactive protein
 - e. Elevated erythrocyte sedimentation rate
 - f. Positive lab test for *C. trachomatis* or *N. gonorrhoeae* infection
 3. Specific criteria
 - a. Positive biopsy of endometrium showing endometritis
 - b. Evidence of PID on laparoscopy
 - c. Ultrasound (transvaginal) or MRI shows fallopian tubes that are thick and filled with fluid; may be free fluid in the pelvis or a tubo-ovarian complex.
-

Differential diagnosis of PID

Acute intermittent porphyria
 Appendicitis
 Endometriosis
 Ectopic pregnancy
 Gastroenteritis (as due to *Yersinia enterocolitica* or *Campylobacter fetus*)
 Henoch-Schonlein syndrome
 Hemolytic-uremic syndrome
 Inflammatory bowel disease
 Mesenteric lymphadenitis
 Ovarian cyst (with or without torsion or rupture)
 Pyelonephritis
 Other

►Tab. 18.6 notes CDC-recommended treatment options that seek to provide polymicrobial antibiotic coverage to contain the infection (including facultative and anaerobic bacteria) and prevent sequelae. In those with mild to moderate disease, oral and intravenous therapy are considered equally effective. For those receiving intravenous antibiotics, therapy may be stopped after 24 hours of clinical improvement with continuation of doxycycline for 14 days total. Intravenous (IV) doxycycline infusion can be very painful, and oral doxycycline may thus be preferred. Anaerobic coverage should be included in the presence of a tubo-ovarian abscess.

Tab. 18.6: Antibiotic management of PID (1).

Oral

- Ceftriaxone 250 mg IM in a single dose *or* cefoxitin 2 g IM in a single dose and probenecid 1 g orally concurrently *or* other third-generation cephalosporin (as ceftizoxime or cefotaxime)

Plus

- Doxycycline 100 mg orally twice a day for 14 days with or without metronidazole 500 mg orally twice a day for 14 days

Parenteral

- Regimen A

Cefotetan 2 g IV every 12 hours *or* cefoxitin 2 g IV every 6 hours *plus* doxycycline 100 mg orally *or* IV every 12 hours

- Regimen B

Clindamycin 900 mg IV every 8 hours *plus* gentamicin loading dose IV or IM (2 mg/kg body weight) followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3–5 mg/kg) can be substituted.

18.7 Fitz-Hugh-Curtis syndrome

The Fitz-Hugh-Curtis Syndrome (perihepatitis) is due to inflammation of the liver capsule after genital infection with *N. gonorrhoeae* or *C. trachomatis*. There may or may not be symptomatic genital infection at the time the perihepatitis presents. Acute, severe, and knife-like right upper quadrant pain develops with or without right shoulder pain, right costal margin friction rub, and abdominal rebound or rigidity. Fever, nausea, emesis, hiccups, pleurisy, and pleuritic chest pain may also occur. The erythrocyte sedimentation rate (ESR) is elevated, and the liver function tests (LFT) are usually normal, though transient rise in LFTs has been reported. A laparoscopy will usually demonstrate the perihepatic inflammation and/or presence of the adhesions between the anterior abdominal wall and the liver. Most acute cases will have a positive cervical culture for gonorrhea or chlamydia. The liver enzymes (if elevated) are normalized quickly after antibiotic treatment.

Differential diagnosis includes other sources of right upper quadrant pathology, including cholecystitis, pancreatitis, peptic ulcer disease, hepatitis, pyelonephritis, pleurisy (with or without pneumonia), pulmonary embolism, pleurodynia, herpes zoster, and others. A rapid response to antibiotics is usually noted. Some individuals develop chronic pain due to the adhesions, requiring lysing of them for pain relief via laparoscopy. The correct diagnosis is based on a high index of suspicion in a sexually active female with right upper quadrant and gonococcal or chlamydial infection, which improves with antibiotics or is confirmed via laparoscopy. Treat as per PID management guidelines (►Tab. 18.6) via the 2010 CDC STD treatment guidelines (1).

18.8 DGI

Approximately 3 percent of women and 1 percent of men with gonorrhea may develop septicemia leading to DGI, with evidence of dermatitis, arthritis or tenosynovitis, perihepatitis, meningitis, endocarditis, and others; the most common form of DGI is the dermatitis-arthritis syndrome. The most common form of dermatitis is the vesicular pustule (4 mm to 2.5 cm) which is noted within 2–4 weeks of the urethral gonorrhea and is found as 2–9 lesions on the extensor surface of the hands, dorsal surface of the ankles and toes, and other areas. They appear in crops or at different times and probably represent gonococcal embolization or an immunologically mediated vasculitis. A positive Gram stain and/or culture of the lesions may be noted. The pustules develop into pigmented lesions and clear without scarring in 1–2 months. Sometimes purpuric macules on the palms or soles appear, as well as hemorrhagic bullae in various areas, or a petechial rash over the hands, feet, and ankles. The oral mucosa and scalp are usually spared. Secondary lymphadenopathy does occur.

A polyarthritis or monoarthritis (tenosynovitis) has been described in the medical literature, but the pattern is variable. Many joints may be involved, including the knee, ankle, wrist, the small joints of the hands or feet, sternoclavicular joints, and others. The monoarticular type often affects the knee. The joint fluid is frequently opaque or slightly cloudy, has a poor mucin clot, increased protein and variable leukocytosis (10,000–100,000 per cu mm). Gonococcal dermatitis (see section 18.7) and elevated

ESR often occur. Tenosynovitis (dorsa of hands or feet, wrists, Achilles tendon, and others) also occurs. The ESR rate falls with effective therapy (as ceftriaxone 1 gram IV daily for 7–10 days). Joint destruction occurs without treatment. The urethral discharge may be minimal or absent when DGI symptoms appear. Gonococcal arthritis dermatitis syndrome is the main type of DGI and is the main cause of bacterial arthritis in sexually active teenagers and young adults. Gonococcal osteomyelitis is a rare complication of gonococcal arthritis. Rapid response to therapy is usually noted but is slow if purulent synovial effusions are noted. Osteomyelitis requires a much longer treatment regimen.

Treatment of DGI is usually with ceftriazone (1 gram IM or IV) every 24 hours until improvement develops, often given for at least a week or more; alternative antibiotics are cefotaxime (1 gram IV every 8 hours) or ceftizoxime (1 gram IV every 8 hours). After 24 to 48 hours of clinical improvement, therapy can be switched to oral cefixime. Patients should also be treated for presumed *C. trachomatis*. See the 2010 STD guidelines from the CDC (1).

18.9 HSV

Infection HSV, type I, causes 10–20 percent of genital herpes, while type II causes the majority. Type I can lead to herpes labialis, keratitis, eczema herpeticum, and gingivostomatitis (10,11). There is an increase in HSV-1 anogenital herpes in young women and MSM. More than 50 million individuals in the United States (more than 500 million worldwide) have genital HSV infection, and the highest incidence is in the adolescent and young adult age group. Only one-quarter of those with HSV-2 infection have known genital disease, and most cases are acquired from someone without known disease because of viral shedding in both asymptomatic and symptomatic persons. Latency and reactivation phenomena are classic with HSV infections.

A number of clinical presentations for HSV-2 are noted, including a first clinical episode that is primary (with no prior HSV history and being sero-negative for testing), a nonprimary first clinical episode (with a first recognized clinical episode and sero-positive for HSV-1 and HSV-2), recurrent clinical episodes (with recognized, repeat clinical episodes and sero-positive for HSV-2), and asymptomatic presentation (with no recognized clinical episode but sero-positive for HSV-2).

Classic clinical HSV-2 in the female presents as a cervicitis or vulvovaginitis that has a mucopurulent discharge in association with vulvar ulcerations. There can be oropharyngitis, urethritis, and proctitis. Typically, there is itching or hyperesthesia followed by a number of small-group vesicles with erythematous bases that change or rupture into small shallow tender ulcers. These painful lesions can persist for 3 to 14 days before disappearing without scarring. The lesions may arise on various locations of the genitals (vulva, cervix, penis, periurethra) but can spread to the vaginal, scrotum, urethra, anus, perianal areas, rectum, thighs, or buttocks. One or more deeper ulcers can be seen with primary disease in association with fever, headache, general malaise, anorexia, and inguinal lymphadenopathy. Uncommon complications to herpes genital infection include erythema multiforme, meningitis, ascending myelitis, radiculomyelitis (with acute urinary retention), and hepatic failure.

The following box lists supportive laboratory data; cell culture and PCR (NAAT) are the recommended HSV tests for symptomatic patients. The Giemsa or Wright stain can reveal balloon cells with intranuclear bodies or multinuclear giant cells with electron microscopy. A Papanicolaou (Pap) smear can reveal multinuclear giant cells; these can also be seen in varicella and herpes zoster. Those with genital, anal, or perianal ulcers should be screened for syphilis and herpes; consider *H. ducreyi* if this is locally prevalent. Laboratory testing for syphilis includes dark field examination (at least one daily for 3 days) and syphilis serology (vida infra). Management of herpes labialis includes oral or topical antiviral agents, sunscreen, zinc oxide cream, and topical anesthetic agents. ►Tab. 18.7 lists recommended antiviral treatment for HSV genital infection. Topical antiviral therapy should be avoided with HSV genital infections. Famciclovir and valacyclovir have greater oral bioavailability and may offer the convenience of less frequent dosing compared to oral acyclovir. Antiviral treatment does not eliminate latent virus. Research is ongoing with recombinant glycoprotein vaccines being developed.

Tab. 18.7: Antiviral management for HSV genital infection (1).

-
1. First episode (continue over 10 days if lesions not fully resolved)
 - a. Acyclovir, 400 mg, orally, three times a day for 7–10 days, or
 - b. Acyclovir, 200 mg, orally, five times a day for 7–10 days, or
 - c. Valacyclovir, 1 gram, orally, two times a day for 7–10 days, or
 - d. Famciclovir, 250 mg, orally, three times a day for 7–10 days
 2. Recurrent episodes (shortens duration of lesions)
 - a. Acyclovir:
 - 800 mg, orally, two times a day, for 5 days
 - 400 mg, orally, three times a day for 5 days
 - 800 mg, orally, three times a day for 2 days

Or
 - b. Valacyclovir
 - 1 gram, orally, once a day for 5 days
 - 500 mg, orally, twice a day for 3 days

Or
 - c. Famciclovir
 - 125 mg, orally, two times a day for 5 days or
 - 1000 mg, orally, twice over one day or
 - 500 mg orally; then 250 mg orally twice a day for 2 days
 3. Suppressive management (reduces frequency of recurrences)
 - a. Acyclovir, 400 mg, orally, two times a day, or
 - b. Famciclovir, 250 mg, orally, two times a day, or
 - c. Valacyclovir, 1 gram or 500 mg, orally, once a day (valacyclovir at 500 mg may be less effective for those ≥10 episodes/year)
-

Supportive laboratory data for genital herpes simplex infection

Cell culture
 PCR testing (NAAT)
 HSV-specific glycoprotein G2 (HSV-2) and G1 (HSV-1)
 Giemsa stain or Wright stain (Tzank test)
 Pap smear
 Electron microscopy reveals viral herpetic particles

18.10 *T. vaginalis*

There are 5 million STD cases in the United States due to trichomoniasis; half are asymptomatic in females, and it is found in 5 percent of males attending an STD clinic (15,16,17,18,19). Prevalence in 18 to 26 year olds is 2.8 percent in females and 1.7 percent in males. Three trichomonas species are identified in humans: *T. buccalis* in the mouth, *T. hominis* in the gastrointestinal tract, and *T. vaginalis* in the genital tract. *T. vaginalis* is a unicellular, flagellated protozoan that commonly causes a vaginitis and cervicitis with secondary vulvitis and urethritis. *T. vaginalis* is spread sexually including through close genital contact. It has been noted to survive for a few hours in wet towels. The incubation period is 4–30 days, after which genital tract infection occurs involving the vagina, cervix, bladder, urethra, Skene's (periurethral) and Bartholin's glands.

The vagina is erythematous and contains a profuse, greenish (or gray or yellow-green), frothy ("bubbly") or malodorous discharge. It is intensely pruritic with a pH of 5.0–5.5 or higher. A mucopurulent or turbid vaginal discharge may be noted in 10 to 15 percent, but this can also be seen with herpes simplex infection, chlamydia infection, and gonorrhea. "Strawberry marks" (vaginocervical ecchymosis, 2% of infections) and swollen vaginal papillae are classic for trichomoniasis. There may be vaginal bleeding with genital trauma from coitus or even touching the genital area with a cotton swab. Dysuria is frequent and severe cases may present with low abdominal pain as well as excoriation of the vulva or inner thighs. Adolescents may be more prone to severe symptomatology than adults. Postpartum trichomoniasis has been noted with fever, leukorrhea, and endometritis. A prolonged carrier state is possible and may be associated with menses – induced, acute exacerbations, as well as chronic pelvic congestion, dysmenorrhea, and menorrhagia.

The differential diagnosis includes vulvovaginitis due to *N. gonorrhoeae*, *Candida albicans*, or BV. The presence of the leukorrhea or cervical infection is not enough for diagnosis. For example, what appears as an "inflamed" cervix may be a benign cervical erosion in which the endocervical columnar epithelium spreads out of the cervical canal, forming a border around the external os.

The saline drop (sensitivity of 60%–70%), Pap smear, and/or culture (most sensitive) can aid with the diagnosis. A saline preparation reveals numerous pear-shaped motile microbes which are unicellular flagellated organisms twice the size of a white blood cell. These microbes may not be seen in chronic carriers if urine is the sample study

or if the patient used a chemical douche prior to the exam. The lubricant used on the speculum can also hinder this test result. These organisms can also be noted in urine samples or on Pap smears. However, the Pap smear can result in false negative – as well as false positive results. Cultures are possible in some laboratories; these are helpful in suspicious cases with multiple negative saline preparations. FDA-cleared tests include OSOM Trichomonas Rapid Test (color immunochromatographic [dipstick] technology) and Affirm VP III; the latter is a nucleic acid probe test for *T. vaginalis*, *C. albicans*, and *G. vaginalis*.

Treatment is with nitroimidazoles as metronidazole and tinidazole. Metronidazole can be given as a single 2-gram dose, or tinidazole is given at 2 grams orally in one dose; an alternative regimen for metronidazole is a 7-day oral course (500 mg twice a day). Those who drink alcohol need to avoid this substance during treatment and for up to 24 hours after taking metronidazole and 72 hours after taking tinidazole. Treatment with metronidazole gel should be avoided.

Follow-up is not necessary if the clinical symptoms rapidly resolve while the uncommon resistant infection (not reinfection) can be treated with the 7-day course (500 mg BID) of metronidazole; if the infection is still not resolved, 2 grams (single dose) of metronidazole is given once a day for 3–5 days (1). Vaginal infection is associated with adverse pregnancy outcomes and pregnant patients with *T. vaginalis* vaginitis can be treated with the single 2-gram dose regimen of metronidazole. Those with an immediate-type allergy to metronidazole can be treated with desensitization. Resistance to nitroimidazoles remains limited.

Metronidazole does have numerous side effects including monilial vaginitis, confusion, ataxia, nausea and anorexia, headache, dizziness, transient neutropenia, metallic taste, dermatitis, dry mucosal surfaces, urine discoloration, and peripheral neuropathy. Flushing and nausea with emesis occurs when metronidazole is combined with alcohol due to a disulfiram effect. The single 2-gram dose may reduce many of the side effects for the disulfiram effect. Tinidazole side effects are similar to metronidazole but also include postmarketing reports of severe dermatological reactions including erythema multiforme and Stevens-Johnson syndrome. As noted, avoid alcohol for 72 hours after taking tinidazole.

18.11 BV

In this sexually associated (or enhanced) infection, there is an increased growth of anaerobic bacteria in the vagina, including *G. vaginalis*, *Mobiluncus* species, *Bacteroides* species, *Prevotella* species, *Ureaplasma*, and others; *Mycoplasmas hominis* is also noted, while lactobacilli are reduced. BV induces a vaginitis characterized by a nonitchy, gray-white, frothy, malodorous vaginal discharge with a pH usually less than 4.5; specific cervical or bladder infection is not found. BV can be noted in as many as 50 percent of sexual assault victims evaluated within 72 hours of the assault (23). Transient *G. vaginalis* bacteremia has also been seen, usually associated with delivery or abortion. In sexually active individuals the presence of BV also increases the risks for gonococcal, trichomonal, and chlamydial genital infection in addition to HIV and HSV-2. The frequency of coital behavior and numbers of sexual partners may be factors for BV acquisition in some females.

Clinically, the vaginal discharge, vaginal pH, Whiff test, and wet mount for clue cells are used for the diagnosis of BV. Gram stains of vaginal fluid, typically only obtained in research studies, reveal decreased lactobacilli and increased anaerobic bacteria. A saline preparation or Gram stain of the leukorrhea identifies clue cells – epithelial cells covered (“studded”) with many gram-negative bacilli; a positive sample is when 20 percent or more of the epithelial cells are covered with bacteria. The sensitivity of the wet mount test is 70–90 percent (vs. 75%–80% for the low pH) and specificity is 95–100 percent (vs. 60%–70% for the low pH test). A less proven test is producing an amine-like odor when a small amount of this discharge is mixed with 10 percent potassium hydroxide (KOH) solution (Whiff test). There is also a DNA probe to detect high concentrations of *G. vaginalis*; the Affirm VP III test, as noted earlier, can detect *G. vaginalis*.

►Tab. 18.8 lists the 2010 CDC recommended treatment options for symptomatic BV. Follow-up of nonpregnant patients with BV who resolve with recommended treatment is usually not necessary. There are no recommendations to treat the male partner of the female with BV, and it remains debated whether or not to treat asymptomatic BV in pregnant women without a previous history of preterm delivery, since it does not prevent preterm labor and delivery.

18.12 HPV

HPV is a double-stranded DNA virus that accounts for 20 million or more STDs in the United States (6,7,8,9). HPV subtypes are identified with an immunoblot typing system; more than 100 types are now recognized, including these often associated with clinical symptomatology with approximately 40 that infect the genitals and at least 14 that are oncogenic. Types 6 and 11 lead to genital condylomas, and type 16 is the most

Tab. 18.8: Management of BV (1).

Preferred (nonpregnant, nonlactating)

- Metronidazole (500 mg BID orally for 7 days) *or*
 - Clindamycin cream (2%) (one full applicator [5 grams] intravaginally before bedtime for 7 days)
- or*
- Metronidazole gel (0.75%) (one full applicator [5 grams] intravaginally, once a day for 5 days)

Alternative (nonpregnant, nonlactating)

- Tinidazole (2 grams orally once daily for 2 days) *or*
- Tinidazole (1 gram orally once daily for 5 days) *or*
- Clindamycin (300 mg orally twice a day for 7 days) *or*
- Clindamycin ovules (100 mg intravaginally once at bedtime for 3 days)

Preferred (pregnant)

- Metronidazole (500 mg orally, twice a day, for 7 days) *or*
 - Metronidazole (250 mg orally, three times a day, for 7 days) *or*
 - Clindamycin (300 mg orally BID for 7 days)
-

common cause of anogenital cancer. Other oncogenic types include 18,31,33,35,39, 45,51,52,58,59,68,73, and 82. There is an incubation period of a few weeks to several months; it infects basal epithelial cells. It is sexually transmitted and is often associated with other infections (*C. albicans*) and STDs (as trichomoniasis and gonococcal cervicitis).

HPV is noted in 3–8 percent of unselected young female patients; 25–50 percent of patients seen in an STD clinic were noted to have HPV using colposcopy. As many as 70 percent of these particular patient's sex partners displayed warts or had them before. Biologic risk factors for acquiring HPV include the presence of cervical ectopy, micro-trauma, and immature immune response capacity. Most HPV infections are acquired early in the sexual life of the patient and youth may be more vulnerable to this infection than adults, from a biological viewpoint. Viral protein transcription leads to various HPV manifestations: warts, dysplasia, and cancer. The HPV wart lesion may involve any part of the genitals (including the vagina, urethra, bladder, or anal canal), and the infection can be very extensive. They seem to worsen in individuals with vaginal discharge, poor hygiene, heavy perspiration, and pregnancy. Lesions resistant to treatment are reported in some individuals with insulin-dependent diabetes mellitus and with immunosuppressive disorders.

Most HPV infections in humans are asymptomatic and are only detected by colposcopy or Pap smear testing. Thus, the prevention of HPV infections with the HPV vaccines is recommended for females and males from ages 9 to 26 years of age "in contrast" to treating the warts or cancer that develop after the infection. The bivalent vaccine (Cervarix) offers protection against HPV types 16 and 18, while the quadrivalent vaccine (Gardasil) offers protection against HPV types 6,11,16, and 18. The quadrivalent vaccine provides protection against the two most common HPV strains that cause genital warts. The vaccine is a three-dose series, and common side effects include fever, injection site reactions, arthralgias, and fatigue. Syncope sometimes associated with tonic-clonic movements or other seizure-like activity has been reported, and observation of the patient for 15 minutes after administration is recommended.

The Bethesda system LSIL (low-grade squamous intraepithelial lesions) corresponds to the World Health Organization CIN (cervical intraepithelial neoplasia) I classification versus HSIL (high-grade squamous intraepithelial lesion), which reflects CIN II and III. HPV is necessary for the development, maintenance, and progression of CIN; HPV is linked to cervical and vulvar neoplasia as well as anal cancer, penile cancer, and oropharyngeal cancer. Though the timing of starting Pap smears is controversial, the American College of Obstetricians and Gynecologists recommends initial Pap smear screening at age 21 regardless of the sexual history.

The differential diagnosis of HPV warts includes molluscum contagiosum, condyloma lata (syphilis), skin tags (peri-anal), urethral prolapsed, and pearly penile papules. The presence of squamous papillomas in moist mucocutaneous areas of the external genitalia and perianal regions is usually sufficient for its diagnosis. Biopsy is confirmatory and mandatory if lesions are resistant to podophyllin therapy. Voiding cystourethrography will demonstrate if intraurethral spread has occurred. Colposcopy is used by some clinicians but there are problems with access and cost. Cytology (Pap smear) is the most practical diagnostic tool but has low sensitivity and specificity. Molecular diagnostic modalities include in situ hybridization, dot-blot (commercially

available ViraPap/Vira Type), Southern blot, and PCR. The PCR is the most sensitive test for HPV. Hybrid Capture is FDA approved to evaluate 14 high-risk or cancer-associated HPV types.

►Tab. 18.9 lists the therapy options for warts. Therapy of concomitant STDs and using 10–25 percent tincture of podophyllin (podophyllum resin in tincture of benzoin) on the lesions may be helpful, especially if the areas are less than 2 cm in diameter. White petrolatum jelly may be then added and this mixture of podophyllin, and white petrolatum jelly is thoroughly washed off in 2–4 hours. There are other techniques for using podophyllin, but these all stress that normal tissue must be protected from the caustic podophyllin that induces pain. Weekly applications may be necessary and seems to be most effective with moist, fleshy, sessile genital warts. The role of more frequent application is under study, and the goal of treatment is to remove the symptomatic wart. Regression is noted in 79 percent within 2 years, and there is no evidence that treatment of overt warts affects the development of cervical cancer. Persistent infections are associated with smoking, other STDs, multiple partners, and immunosuppression states.

Podophyllin is not used for cervical warts or for pregnant patients. If there is not regression after four weekly trials, other methods are used. Unfortunately, there is no treatment proven to eradicate this virus and no specific regimen to always remove the warts and prevent recurrences. In addition, no one treatment suites all patients and therapy should be individualized. The use of topical chemotherapeutic agents (as 80%–90% trichloroacetic acid [OK for pregnancy and mucosa] or 5-fluorouracil) has been used as alternatives to topical podophyllin treatment. Podofilox (0.5%) is available for home use; others include Imiquimod 5 percent cream and Sinecatechins 15 percent ointment. None of the at-home treatments have been adequately assessed in pregnancy.

Tab. 18.9: Treatment options for external genital warts (1).

A. Topical application

- Patient applied:
 - Podofilox 0.5% solution or gel
 - Imiquimod 5% cream
 - Sinecatechins 15% ointment
- Provider administered:
 - Cryotherapy with liquid nitrogen or cryoprobe
 - Podophyllin resin 10%–25% (in compound tincture of benzoin)
 - Trichloroacetic acid or bichloroacetic acid 80%–90%

B. Other

- Surgical removal of warts
 - Intralesional interferon injection
 - Laser surgery
 - Topical cidofovir
-

Methods that have been recommended as alternatives to podophyllin therapy include curettage, electrocauterization, loop electrosurgical excision procedure, alpha interferon, surgical excision, and cryotherapy (with liquid nitrogen or solid carbon dioxide). Immunotherapy with an autogenous vaccine (prepared from excised warts) has been attempted but is without proven success. Laser treatment has also been used with success. Careful follow-up of these patients is important, due to the link of this virus to cervical cancer and other cancers.

18.13 Vulvovaginitis

Puberty exerts a profound estrogen effect on the female genital tract that produces a thicker, longer vagina with an adult effect on the vaginal cell count: approximately 60 percent superficial cells, 31 percent intermediate, and 9 percent parabasal. The pH is in the acidic range (5.0 to 5.5) due to lactic acid production partially from the presence of lactobacilli (see the following box, "Normal Flora of the Vagina after Puberty"). One result of this thickened, acidic vaginal milieu is increased protection against infection. Vulvovaginitis tends to be due to specific causes (►Tab. 18.10), many of which are covered earlier in this chapter. The presence of certain identified pathogens (i.e. *N. gonorrhoeae*, *T. vaginalis*, *C. albicans*, *G. vaginalis*) does not always mean asymptomatic infection exists; sometimes a triggering mechanism (often not known) must occur before overt symptomatology occurs.

Tab. 18.10: Causes of vulvovaginitis.

-
1. Leukorrhea and/or vaginitis	a. Physiologic leukorrhea b. <i>C. albicans</i> vaginitis c. BV d. <i>T. vaginalis</i> vaginitis
2. Cervicitis due to	a. <i>C. trachomatis</i> b. <i>Ne. gonorrhoeae</i> c. HSV
3. Miscellaneous	a. Allergic vulvovaginitis b. Foreign body vaginitis c. Vulvar ulcerations (herpes, syphilis, chancroid, lymphogranuloma venereum granuloma inguinale, amebiasis, Behcet's syndrome, others) d. Vulvitis (scabies, molluscum contagiosum, pediculosis, warts [HPV], tinea, psoriasis, furunculosis, pruritus vulvae, others)
-

Normal flora of the vagina after puberty

Döderlein's lactobacilli
 Enterobacteriaceae
Bacteroides fragilis
Neisseria sicca
 Streptococci (including group B)
 Staphylococci
 Diphtheroids
C. albicans
 Other yeasts
 Other anaerobic bacteria
 Other microbes

18.14 Physiological leukorrhea

Physiologic leukorrhea refers to a normal increase in vaginal discharge (leukorrhea) due to puberty-stimulated increase in estrogen production; it can also be noted in the first few days or weeks after birth in the female newborn due to ematernal estrogen. In early puberty the vaginal discharge is from mucus secretion of the cervical columnar epithelium, vaginal wall fluid transudation, and multiple gland stimulation (i.e. Bartholin's, sebaceous, and sweat). Classically it initiates several weeks or months prior to menarche and is variable in amount usually until regular menstruation is established.

The leukorrhea is typically clear, sticky, and nonirritating and may increase during pregnancy or even during sexual arousal. A saline preparation of the vaginal fluid reveals normal vaginal cytology without leukocytes or pathogenic bacteria. Cultures of the vaginal fluid are not necessary but, if obtained, are negative. The young adolescent female may be concerned that it is due to genital injury or an STD. Nylon undergarments absorb the fluid poorly in contrast to the excellent absorptive powers of cotton undergarments. Good perineal hygiene is recommended with normal baths, and medication is to be avoided; inadvertent use of medication can lead to such sequelae as dermatitis medicamentosa.

18.15 *C. albicans*

Vulvovaginal candidiasis (VVC) is a common cause of vulvovaginitis not classified as an STD and due to *C. albicans* in 80–90 percent, *Torulopsis glabrata* in 10–15 percent, and *C. parapsilosis* in 1–2 percent. ▶Tab. 18.11 lists various precipitating factors in the development of recurrent or chronic VVC. VVC typically presents with vagino-vulvar erythema, intense pruritis, and a whitish, cheese-like vaginal discharge with a pH of 3.8 to 5.0 (typically <4.5). Itchiness with erythema and decreased leukorrhea may occur if the infection is precipitated by antibiotics; more leukorrhea occurs if VVC

Tab. 18.11: Precipitating factors for chronic or recurrent VVC.

-
1. Removal of normal vaginal flora with *Candida* overgrowth due to broad-spectrum antibiotics
 2. Reduction of host defense mechanism
 - a. Chronic illness
 - b. Steroids
 - c. Aging
 - d. Severe iron deficiency anemia
 - e. Immune disorders
 3. Chronic *Candida* exposure
 - a. Infected sex partner
 - b. Contaminated soaps
 - c. Intestinal reservoir
 4. Increase in heat or moisture
 - a. Obesity
 - b. Tight nylon undergarments
 5. Lower the pH
 - a. Pregnancy
 - b. Oral contraceptives
 - c. Diabetes mellitus
-

develops during pregnancy. Increase in the discharge may occur before and after menstruation but decrease during menstruation.

Other symptoms that may occur include urinary frequency, dysuria, and dyspareunia. There may also be fissuring, lichenification, and secondary bacterial infection over the perineal areas or legs (including the thighs). Skene's glands and endocervical glands may also be infected. The presence of thickened, bronzed, or dull red skin over the labia or groin suggests chronic infection. Dermatophytids (Monilids) can develop as very pruritic, but sterile lesions at the sides of the fingers and hands. Laboratory testing reveals a vaginal secretion with a pH under 5.0, while a 10 percent KOH preparation shows hyphae (mycelia), pseudo-hyphae (nondetached buds), yeast (oval cells), and possibly white blood cells; the exam is negative for clue cells and trichomonads. Culture can also be accomplished.

The only FDA-approved oral medication is fluconazole that is given as 150 mg tablet (►Tab. 18.12). A number of azole agents are available as topical agents, as noted in ►Tab. 18.12, that are oil-based and thus may weaken latex condoms and diaphragms. Topical azoles are considered more effective than nystatin and are recommended for use during pregnancy; short courses (1–3 days) are as effective as longer courses. *C. albicans* can be found in as many as 20 percent of females without VVC symptoms, and antifungal treatment is usually not indicated in this situation. Treatment of sexual partners of females with symptomatic VVC is not recommended unless she has recurrent or chronic disease. A minority of male sex partners of females with VVC may develop balanitis that usually resolves with topical antifungal agents; other potential causes of balanitis include HSV and primary syphilis.

Tab. 18.12: Management of VVC.

-
1. Oral agent: fluconazole* (150 mg oral tab) in a single dose
 2. Clotrimazole:
 - cream (1%) (5 grams) intravaginally for 7–14 days or
 - cream (2%) (5 grams) intravaginally for 3 days
 3. Miconazole nitrate:
 - vaginal cream (2%) once daily (5 grams) for 7 days
 - vaginal cream (4%) once daily (5 grams) for 3 days
 - 200 mg vaginal suppository, one suppository for 3 days
 - 100 mg vaginal suppository, one suppository for 7 days
 - 1,200 mg vaginal suppository – use once
 4. 2% butaconazole nitrate (Femstat) cream – 5 grams given intravaginally for 3 days
 5. Others include tioconazole and terconazole* and as topical agents
-

*Prescription only.

Females with recurrent VVC due to *C. albicans* may be managed with a short course of fluconazole (100 to 200 mg every 3 days for 3 doses) or 1 to 2 weeks of topical agents; longer “maintenance” antifungal treatment may be considered (1). Most have uncomplicated VVC. Complicated VVC is not well understood and involves those females with recurrent VVC (four or more episodes per year – found in <5%), severe VVC, non-*albicans* candidiasis, or those with uncontrolled diabetes mellitus or immunosuppression states. Females with non-*albicans* VVC can be treated with nonfluconazole azole drugs (oral or topical) for 7 to 14 days. Numerous drug interactions exist with oral azole agents due to cytochrome P450 enzyme metabolism and inhibition. A patient’s medication regimen should be reviewed for drug interactions before initiating an oral azole medication. If further infection occurs, use boric acid (600 mg) in a gelatin capsule intravaginally, once a day, for 14 days (1).

18.16 Miscellaneous STDs

Many other STDs are noted in youth. HIV is discussed in section 18.17.1. Reiter syndrome is considered in the rheumatology chapter (chapter 13). Group A streptococci can cause a vaginitis in prepubertal females after transmission by sexual contact or autoinoculation from the pharynx; management is with 10 days of penicillin. ►Tab. 18.13 outlines treatment for pediculosis pubis (due to *Phthirus pubis*) and scabies (due to *S. scabiei*). Increasing resistance with permethrin and pyrethrins may require use of malathione if treatment failure occurs for pediculosis pubis. Due to the neurological toxicities associated with lindane, permethrin and ivermectin are considered first line treatments for scabies. Lindane and ivermectin should not be used during pregnancy.

Pinworms (*Enterobius vermicularis*) may cause rectal and vaginal irritation as well as pruritus. The worms may be found in the perianal area at night or identified with the cellophane tape test. Treat with pyrantel pamoate (nonprescription: 11 mg/kg with maximum of 1 gram orally; repeat in 2 weeks) or with prescription medications:

Tab. 18.13: Treatment options for pediculosis pubis and scabies (1).**A. Pediculosis pubis**

- Permethrin (1% cream rinse – apply to affected areas; wash off in 10 minutes) *or*
- Pyrethrins (with piperonyl butoxide – apply to affected areas; wash off in 10 minutes)

Alternative:

- Malathione (0.5% lotion applied for 8 to 12 hours; wash off) *or*
- Ivermectin (250 mcg/kg orally; repeat in 2 weeks)

B. Scabies

- Permethrin* (5% cream – apply from neck down; wash off in 8 to 14 hours) *or*
- Ivermectin* (200 mcg/kg orally; repeat in 2 weeks)

Alternative:

- Lindane* (1%): 1 oz. (30 gram) of cream applied in a thin layer to all areas from the neck down; wash off thoroughly after 8 hours; do not apply directly after bathing.

*Prescription only.

mebendazole (100 mg tablet once and may need to repeat in 2 weeks) or albendazole (400 mg tablet and repeat in 2 weeks; unlabeled indication). All family members in close contact with the patient should also be treated. See the dermatology chapter (chapter 1) for consideration of other conditions that may be associated with sexual behavior, such as tinea cruris, contact dermatitis, and molluscum contagiosum.

LGV is an STD due to infection with *C. trachomatis* (serotypes L1, L2, and L3) with an incubation period of 3 to 30 days; it causes inguinal lymphadenopathy (buboes) that is painful as well as genital ulcers and severe ulcerative proctitis (proctocolitis). The primary lesion may be a small red erosion (often missed) with fever, malaise, myalgias, and arthralgias. Unilateral lymph nodes above and below the inguinal ligament are called the “groove” sign. Untreated LGV can lead to bowel obstruction, bowel perforation, rectal strictures, and even death. Molecular testing is available to establish a diagnosis of LGV while treatment involves doxycycline (100 mg orally, twice daily, for 21 days); an alternative plan is erythromycin base (500 mg orally QID for 21 days). Erythromycin should be used during pregnancy and in lactating females.

Chancroid (due to *H. ducreyi*) has an incubation period of 3 to 14 days and presents with a small, painful, erythematous papule that classically erodes into a ragged ulcer with undetermined edges; there is usually painful, often unilateral, inguinal lymphadenopathy that may be suppurative. Laboratory data may include culture (often difficult to obtain) and PCR testing. Management is with ceftriaxone (250 mg IM), ciprofloxacin (500 mg BID for 3 days) or azithromycin (1 gram orally); an alternative plan is erythromycin base (500 mg TID for 7 days). Fluoroquinolones should be avoided during pregnancy and in lactating females.

Granuloma inguinale (donovanosis) is due to infection with *K. granulomatis* (formerly called *Calymmatobacterium granulomatis*) that has an incubation period of 2 to 10 weeks and presents with an erythematous nodule or papule that is usually nonpainful but then ulcerates to form friable, beefy-red granulation tissue; tissue biopsy can note Donovan bodies. Inguinal lymphadenopathy is not usually noted but perilymphatic granulomas (“pseudobubos”) may mimic enlarged lymph nodes. It is treated

with doxycycline (100 mg orally, twice daily, for at least 3 weeks) or 160 mg of trimethoprim with 800 mg of sulfamethoxazole – one tablet orally, twice daily, for 3 weeks. Alternative treatments include ciprofloxacin (750 mg orally, twice a day, for 3 weeks), erythromycin base (500 mg, orally, four times a day for 3 weeks), or azithromycin (1 gram orally, per week, for 3 weeks). In pregnancy, erythromycin is preferred and inclusion of an intravenous aminoglycoside should be considered. Treatment should continue until all lesions have completely healed and relapses can occur despite appropriate treatment.

Syphilis is an STD of antiquity due to *T. pallidum* with an incubation period of 9 to 90 days (average of 3 weeks) (24,25). This pathogenic spirochete gains access via mucosal abrasions during sexual activity with the induction of a local immune response and secondary hematogenous spread. Primary syphilis presents with the classic chancre that is a well-defined, painless, erythematous ulcer with a firm (rubbery) base; there is usually inguinal lymphadenopathy that can be bilateral or unilateral, and typically nontender as well as nonsuppurative.

Diagnosis is with darkfield microscopy to identify the treponemes and serology (nontreponemal tests: rapid plasma reagin [RPR], Venereal Disease Research Laboratory [VDRL]). The sensitivity of RPR or VDRL is higher in secondary syphilis versus primary or latent syphilis; also, RPR and VDRL are associated with false positive results and false negative results (prozone reaction). Direct fluorescent antibody testing (DFA-TP) of smears can also be used if available. Treponemal tests can be used: fluorescent treponemal antibody absorption (FTA-ABS) and microhemagglutination assay (MHA-TP) that remain positive for a lifetime in most (despite treatment). Screen those with a history of exposure to syphilis with an RPR or VDRL and if positive, do a treponemal test (i.e. MHA-TP or FTA-ABS).

The chancre lasts 2 to 6 weeks and will resolve even without treatment. Secondary syphilis appears 6 weeks to 6 months after disappearance of the chancre and can present with a wide variety of constitutional symptomatology in its role as the “Great Imitator”: malaise, fever, generalized lymphadenopathy, hepatosplenomegaly, rhinitis, sore throat, alopecia (“moth-eaten”, patchy), polymorphic rash (with or without involvement of the palms and soles), headache, arthralgias, anogenital condylomata lata, and many others.

The rash of syphilis may begin as a red, macular eruption first on the extremities and trunk; lesions may become elevated with a copper-red hue and involve the palms as well as soles. Plaque-like lesions may be seen that mimic psoriasis while the appearance of rings can mimic tinea corporis. Condyloma lata appear as skin-colored or gray, macerated papules in the perianal or genital area; there can also be mucous patches that present as oval, gray erosions on the genital areas or in the oral cavity. Secondary syphilis can last 2 or more weeks and also resolve without treatment. Later stages can occur that are rarely seen in adolescents, including early latent (within 1 year of infection), late latent (can persist for many years without symptoms), latent syphilis of unknown duration, and tertiary (neurologic, cardiac, gummatous lesions).

Primary, secondary, and early latent stages of syphilis are treated with Benzathine Penicillin G (2.4 million units IM) in one dose; late latent, latent syphilis of unknown duration, and tertiary syphilis (not neurosyphilis) are treated with Benzathine Penicillin G (2.4 million units IM) weekly for 3 weeks. Neurosyphilis should be treated with intravenous penicillin G (18–24 million units per day) for 10–14 days. A patient with

syphilis who is allergic to penicillin is desensitized and treated with penicillin. Alternative treatment in nonpregnant individuals is tetracycline (500 mg, orally, four times a day) or doxycycline (100 mg, orally, twice a day) for 14 days. An acute febrile reaction called the Jarisch-Herxheimer reaction can occur within 24 hours of initiating treatment; this is typically seen in patients with early syphilis and can be managed with antipyretics. See the CDC STD guidelines (2010) for management of syphilis including neurosyphilis, tertiary syphilis, latent syphilis, and congenital syphilis (1).

18.17 Homosexuality and STDs in adolescents

Homosexual behavior may occur during adolescence and eventually, 4 to 6 percent of adults will identify themselves as gay, lesbian, or bisexual. Young adolescents may only find homosexual contact at public places where problems with sexually transmitted diseases (including HIV infection) often exist. Lesbian teens may have sex with males as part of their adolescent sexual experimentation and some are at increased risk of HIV infection as well as other STDs because of coitus with infected males; pregnancy risks also occur in this situation if unprotected sex occurs.

About 25 percent of those with HIV/acquired immunodeficiency syndrome (AIDS) in the United States contracted their infection by the age of 21 years. For those in their twenties with HIV, many, if not most of them, were infected while they were still teenagers or in their early twenties (see section 18.17.1). Even if the adolescent engages in same-sex behavior for economic reasons and not because of being homosexual, risks for STDs remain. Advice regarding testing for STDs includes explaining possible risk factors, treatment options, and discussion regarding confidentiality as well as informing the adolescent's parent, if possible. Advice regarding options for self protection includes safe sex awareness and practice, including sexual abstinence and use of latex condoms. In addition, the adolescent can be taught techniques to handle peer pressure regarding sexual behavior.

The gastrointestinal tract can be involved with acquisition of STD agents in rectal (receptive) sexual activity. Proctitis (rectal inflammation) is noted with anorectal pain, rectal discharge, and tenesmus due to *N. gonorrhoeae*, *T. pallidum*, HSV, *C. trachomatis* (including LGV serovars), and others. In proctocolitis, there is abdominal cramping, diarrhea, and symptoms of rectal inflammation due to various agents (►Tab. 18.14). In enteritis due to various opportunistic agents (►Tab. 18.15), there is mainly abdominal cramping and diarrhea; *Giardia lamblia* is the most common cause in this situation.

Treatment depends on the causative agent(s). In proctitis suspected to be due to *N. gonorrhoeae* treatment is with ceftriazone (250 mg IM) and doxycycline (100 mg orally, twice a day for 7 days) to cover *C. trachomatis*. Consider herpes and LGV serovars as causative of rectal ulcers and treat accordingly; use 3 weeks of doxycycline (100 mg orally, twice a day) for LGV treatment. See the 2010 CDC STD management guidelines (1).

18.17.1 HIV/AIDS

Overall, 1 million individuals are estimated to be infected with the human immunodeficiency virus-1 (HIV-1) in the United States with at least one-third seen in those 15 to

Tab. 18.14: STDs in homosexual/bisexual adolescents.

Urethritis

- *N. gonorrhoeae*
- *C. trachomatis*
- *M. genitalium*
- *U. urealyticum*

T. vaginalis

HSV

Adenoviruses

Pharyngitis

- *N. gonorrhoeae*
- HSV
- *T. pallidum*
- Others

AIDS (persons with HIV infection may acquire various other opportunistic infections not listed)

Genital warts (infection with HPV)

Ectoparasites (*Phthirus pubis**Sarcoptes scabiei*)

Hepatitis

- Hepatitis A, B, C, D, and/or E virus
- Cytomegalovirus
- Epstein-Barr virus

Ulcerative lesions

- Syphilis (*T. pallidum*)
- HSV
- Chancroid (*H. ducreyi*)
- LGV (*C. trachomatis*)
- Granuloma inguinale (*K. granulomatis*)

Enteritis/proctocolitis

- *G. lamblia*
- *Salmonella enteritidis*
- *Entamoeba histolytica*
- *Cryptosporidium* species
- *Campylobacter* species
- *Shigella* species
- *C. trachomatis*
- LGV serovars

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Tab. 18.15: Antiretroviral (ART) medications (partial list).

A. Nonnucleoside reverse transcriptase inhibitors (NNRTIs)

- Efavirenz
- Nevirapine
- Delaviridine
- Etravirine
- Rilpivirine

B. Protease inhibitors

- Atazanavir
- Darunavir
- Fosamprenavir
- Lopinavir
- Saquinavir
- Tipranavir
- Ritonavir
- Indinavir
- Nelfinavir

C. Nucleoside reverse transcriptase inhibitors (NRTIs)

- Abacavir
- Emtricitabine
- Lamivudine
- Tenofovir
- Zidovudine
- Didanosine
- Stavudine

D. Integrase strand transfer inhibitor

- Raltegravir

E. Cellular chemokine receptor 5 antagonist

- Maraviroc
-

29 years of age; approximately half of new infections are found in those under age 25. HIV-2 is prevalent in West Africa. Minority populations suffer disproportionately higher numbers of HIV infection. This virus is transmitted via sexual activity, needle sharing, and also in breast milk.

The main mode of transmission in males having HIV is MSM often with injection drug use, though it can affect any gender or age group that is exposed. The introduction of zidovudine (formerly called azidothymidine [abbreviated AZT]) has greatly reduced mother-to-child transmission at this time. Primary risk categories in adolescent females and young women for HIV infection include heterosexual behavior complicated by injection drug use. Another group of HIV-infected adolescents is those who were infected prenatally and are now in the adolescent age group.

Testing involves use of the HIV EIA/Western blot and should be done according to local state guidelines for HIV testing (1). Generally antibody testing initiates with a screening test such as an EIA, and then reactive screening tests are confirmed with a test such as the Western blot test or immunofluorescence assay. A continued positive test indicates the individual is infected with this virus (HIV) and can infect others. Seroconversion usually occurs within 3 months after infection but may take up to 12 months; a negative testing scheme does not rule out a recent infection. Plasma HIV RNA testing (plasma viral load test) can be obtained in situations when a patient has symptomatology consistent with acute HIV infection but HIV antibody testing is negative or inconclusive. The RNA viral load test measures the amount of free HIV virus (non cell bound) in the infected person. Follow-up testing (i.e. Western blot) can be done in two to four months to confirm HIV infection if the plasma HIV plasma testing indicates HIV infection.

Though most newly diagnosed patients are asymptomatic, some can develop acute retroviral syndrome 2 to 6 weeks after HIV infection before HIV testing becomes positive. A variety of symptoms are noted including fever, malaise, skin rash, and lymphadenopathy. These youth may benefit from early use of anti-HIV medications (antiretroviral drugs) and should be referred to local experts in HIV management. The patient with AIDS has the development of an opportunistic infection or AIDS-defining ailment in one infected with HIV or a drop in the patient's CD4 lymphocyte count to 200 cells/mm³ or less. Those with HIV/AIDS develop a wide, protean variety of potential symptomatology and disorders including generalized lymphadenopathy, hepatomegaly, splenomegaly, failure to thrive, oral thrush, recurrent diarrhea, hepatitis, parotitis, cardiomyopathy, nephropathy, central nervous system disease, lymphoid interstitial pneumonia, recurrent invasive bacterial infections, opportunistic infections, and malignant neoplasms.

ART management is recommended for all those with HIV and AIDS, and referral to local experts in an HIV/AIDS center is recommended to ensure the best treatment for this very complex situation with ever-changing protocols and recommendations. Detailed discussion of management is beyond the scope of this chapter and this book. ART medications are generally divided into five different groups (►Tab. 18.15), and ways to improve adherence to this regimen are listed in ►Tab. 18.16. Detailed instructions are provided at <http://www.aidsinfo.nih.gov>, and it is vital to provide in a program with well-trained health care professionals who adhere to updated protocols. The medications are complex with many side effects and drug interactions. Complicating the overall treatment is the many potential opportunistic infections that may be seen that can be difficult to treat. The patient should make a commitment to a lifetime of treatment that will result in the best possible life span and quality of life, especially as new discoveries are made with research now and in the future.

Classification is based predominantly on the CD4 count and different protocols may be used based on if the patient has or has not received ART (ART-naïve vs. ART-experienced); another important factor is the plasma HIV RNA load. Genotype testing is recommended to optimize regimen selection due to the potential for drug resistance. Early ART treatment helps to protect the patient's sex partner from becoming infected with HIV; correct condom use with all coitus is also important in this preventive scheme. Combination of ARTs is more effective than monotherapy, and protocols generally use three ART drugs from two different classes, such as including two NRTIs

along with a protease inhibitor or NNRTI (►Tab. 18.15). Individualizing therapy is essential, and attempts are made to simplify the treatment protocol to maximize compliance with the treatment protocols (►Tab. 18.16).

Tab. 18.16: Strategies to improve adherence to ART therapy strategies.

Use a multidisciplinary team approach	Nurses, social workers, pharmacists, and medication managers
Provide an accessible, trusting health care team	
Establish a trusting relationship with the patient	
Establish readiness to start ART	
Identify potential barriers to adherence prior to starting ART	Psychosocial issues Active substance abuse or at high risk of relapse Low literacy level Busy daily schedule and/or travel away from home Lack of disclosure of HIV diagnosis Skepticism about ART Lack of prescription drug coverage
Provide resources for the patient	Referrals for mental health and/or substance abuse treatment Resources to obtain prescription drug coverage Pillboxes
Involve the patient in ART regimen selection	For each option, review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of nonadherence
Assess adherence at every clinic visit	Use a simple checklist the patient can complete in the waiting room Have other members of the health care team also assess adherence Ask the patient open-ended questions (e.g. <i>In the last 3 days, please tell me how you took your medicines.</i>)
Identify the type of nonadherence	Failure to fill the prescription(s) Failure to take the right dose(s) at the right time(s) Nonadherence to food requirements
Identify reasons for nonadherence; assess and simplify regimen, if possible	Adverse effects from medications Complexity of regimen (pill burden, dosing frequency, etc.) Difficulty swallowing large pills Forgetfulness Failure to understand dosing instructions <ul style="list-style-type: none"> • Inadequate understanding of drug resistance and its relationship to adherence Pill fatigue Other potential barriers (see list above)

From <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.PDF>. Accessed May 12, 2011. Table 12.

18.18 Conclusions

High rates of unprotected sexual behavior in adolescents result in millions of cases of STDs in the world. This chapter reviews factors inducing high STD rates, specific STDs, and their management based on 2010 CDC STD guidelines. Clinicians should screen all their sexually active adolescent patients for STDs and provide preventive education as well as treatment measures.

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