

VAGINITIS AND SEXUALLY TRANSMITTED DISEASES

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Sexually transmitted diseases (STDs) are among the most common causes of infectious illness in the world. The United States leads industrialized nations in the occurrence of STDs, and after a slight trend downward in the 1990s, there has been an upswing in STDs in the past decade, especially among teenagers. Currently, the annual rate of AIDS diagnoses reported among males aged 15 to 19 years has nearly doubled in the past 10 years, and rates for gonorrhea and syphilis have also risen in this population.¹ In many developing nations, STDs (excluding HIV infection) are the second greatest cause of disability-adjusted years of life lost,² and highly prevalent bacterial and viral STDs may facilitate HIV transmission.³

Of the more than 30 sexually transmitted pathogens that are currently recognized, eight have been identified since 1980, and it seems likely that the full spectrum of STD remains undefined.⁴ Antimicrobial resistance has made treatment of some well-established infections (e.g., gonorrhea) more difficult. Finally, decreasing age at menarche, declining median age of populations in developing countries, delayed marriage, increased global travel and trade, urbanization, migration, war and associated social upheaval, and the dissolution of socially restrictive political systems in the former Soviet Union and, to a lesser extent, China all ensure that STDs will remain a major and probably increasing health problem in coming decades.⁵

For the clinician, the increasing recognition of viral STDs and the emergence of screening for chlamydial infections as a population-based STD control strategy have heightened the importance of familiarity with the management of these common infections. This chapter presents general concepts in the epidemiology and approach to patients with STD and reviews important STD syndromes, including urethritis, vulvovaginitis, mucopurulent cervicitis (MPC), pelvic inflammatory disease (PID), and genital ulcer disease (GUD). Finally, the approach to STDs in men who have sex with men (MSM) and to sexually transmitted enteric infections will be presented. Specific pathogens, including *Chlamydia*, *Neisseria gonorrhoeae*, herpes viruses, and *Treponema pallidum*, are discussed in other chapters. The Centers for Disease Control and Prevention (CDC) issues guidelines for STD/HIV testing and counseling, as well as STD treatment (<http://www.cdc.gov/hiv/dhap.htm>). Clinicians are advised to refer to these guidelines for updated recommendations.^{6,7}

Epidemiology and Transmission Dynamics

The transmission of an STD through a population can be conceptualized mathematically with the formula $R_0 = \beta cD$,

in which R_0 is the average number of secondary cases generated by each primary infection in a population (i.e., the reproductive number), β is the average probability of transmission with each sexual partnership, c is the average number of sexual partnerships formed per unit of time, and D is the mean duration of infection.⁸ For diseases in which each case generates an average of one additional case, R_0 equals 1 and the prevalence remains stable; values less than 1 and greater than 1 are associated with a declining or rising prevalence, respectively.

Although each of the terms in this equation is complex, the simplification that the equation offers can explain a great deal about the distribution of different STDs in a population and provides a framework for conceptualizing STD epidemiology. For example, gonorrhea is thought to be efficiently transmitted ($\beta = 0.5$), but it has a relatively short duration of infection, especially in settings in which medical care and therapy are readily available.^{8,9} Consequently, for the reproductive number to remain 1 or greater, c must be relatively high. Thus, infection tends to concentrate in a population of highly sexually active persons, sometimes referred to as a core group.¹⁰ In part because young people tend to be more sexually active than older people, the incidence of gonorrhea, like that of chlamydial infection, is highest among teenagers and persons in their early 20s. (This is less true of MSM, in whom gonorrhea incidence is less concentrated in the young.) In contrast, herpes simplex virus type 2 (HSV-2) has a very long duration of infection, and R_0 may exceed 1 even in populations with very low rates of partnership change. As a result, the prevalence of genital herpes rises with age, peak incidence likely occurs at a somewhat older age than with *Chlamydia* infection or gonorrhea, and the infection is widely disseminated throughout the population.¹¹

This simple model of STD transmission dynamics focuses on average behavior in a population and the host-parasite relation as determinants of STD epidemiology. However, it neglects the critical role played by variance in sexual behavior and patterns of sexual mixing (i.e., sexual networks) in defining transmission dynamics. The prevalence of STD in a population is in part a function of the extent to which persons who are more sexually active mix primarily with one another (assortative mixing) versus mixing more randomly with others, including persons who are less sexually active.¹² The frequency of concurrent partnerships in a population also exerts a profound influence on STD prevalence; such partnerships allow infections to spread in two directions, connecting groups of people and facilitating rapid transmission of infection.^{13,14}

In eliciting a sexual history, clinicians have traditionally focused on the patient's behavior, asking about the number of sexual partners the patient has had and about the use of condoms. In many cases, however, self-reported behavior is not associated with risk of STD; sexual network factors may

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be more important in defining risk. For example, virtually all studies of selective screening for chlamydial infection have found that self-reported behavior is an insensitive predictor of infection,^{15,16} whereas demographic factors such as age, race, socioeconomic status, source of clinical care, and geography are strongly associated with a variety of STDs.^{17–19} These factors, which reflect the organization of human society and dictate sexual mixing patterns, play a critical role in defining an individual's risk of infection.²⁰ STDs exist within a social context; therefore, clinicians should base their assessment of risk on their practice setting and the patient's social milieu. Persons whose behavior would suggest a low risk of STD can, in fact, be at elevated risk simply by virtue of their sexual network, a population that is often socially determined rather than individually chosen. This knowledge should temper any tendency to entertain stigmatizing stereotypes related to sexual behavior and STD.

STD Prevention

SEXUAL HISTORY AND COUNSELING

What is the best way to elicit a sexual history? Although relatively little research has been done on this question, some general principles can be articulated. In eliciting a sexual history, the clinician must balance the need to collect specific information with the desire to engage the patient in a conversation about sexual risk. Whenever possible, questions should be open ended, allowing the patient to define factors that may have placed him or her at risk for STD (e.g., "What are you doing now, or what have you done in the past, that you think may have put you at risk for a sexually transmitted disease?"). Subsequent questions may be more specific, but the questions should be clear, direct, and phrased nonjudgmentally (e.g., "Do you have sex with men, women, or both men and women?"). Typically, a sexual history should include questions about sexual orientation, the number of sexual partners, the use of condoms, any history of STD, and the sexual repertoire (oral, insertive or receptive anal, and vaginal sex). Persons with HIV or those at high risk for HIV should be asked if they know the HIV status of their sexual partners. Persons with HIV should be asked whether they have informed their partners of their own HIV status.

Clinicians should seek to integrate elicitation of the sexual history with STD prevention counseling. The CDC recommends a client-centered approach to counseling. This approach involves an effort to help patients assess the circumstances and behaviors that place them at risk for STD and then help them commit to a single, defined plan for reducing their risk. Risk-reduction plans should be specific rather than general. For example, a specific goal might be to carry condoms when going out on a date or to ask a specific partner about his or her HIV status rather than the general goals of using condoms all the time or having safe sex all the time.²¹ Client-centered counseling that can be tailored to individual circumstances has been shown to reduce the risk of STDs.²²

STD REPORTING AND SEXUAL PARTNER MANAGEMENT

By law, gonorrhea, syphilis, chancroid, lymphogranuloma venereum (LGV), donovanosis (granuloma inguinale), and,

in most parts of the United States, chlamydial infections must be reported to local health departments. In general, health departments in the United States routinely attempt to ensure the treatment of sexual partners of persons with syphilis; they only sometimes attempt to contact persons reported to have HIV to offer them assistance in notifying their sexual and needle-sharing partners, and they seldom make any routine effort to notify the partners of persons with gonorrhea or chlamydial infection. Some health departments will provide such services if specifically asked to do so by a clinician or a person diagnosed with an STD. Although clinicians should make their patients aware that they may be contacted by public health authorities regarding partner notification, in most instances, it is the responsibility of the diagnosing clinician and the patient to ensure that sexual partners are evaluated and treated. Several recent studies have suggested that giving patients medication to give to their sexual partners is feasible and may reduce chlamydial reinfection rates.^{23–25} However, at present, there are no guidelines that define the circumstances in which this approach to partner management should be employed.

STD SCREENING

Because STDs are often asymptomatic, screening is a critical component of prevention. Recommendations for screening vary according to population [see Table 1].⁷ Data in support of STD screening are strongest for chlamydial infection; chlamydial screening can reduce the rate of PID.²⁶

Urethritis in Men

EPIDEMIOLOGY

Urethritis is one of the most common STD syndromes in men, resulting in an estimated 200,000 initial physician visits in the United States in 2000.²⁷ The syndrome is typically divided into urethritis resulting from infection with *N. gonorrhoeae* and nongonococcal urethritis (NGU). Rates of gonococcal urethritis in most developed nations have declined dramatically over the past 20 years, although rates in the United States and Europe now appear to be rising again, particularly among MSM.²⁸

ETIOLOGY AND MICROBIOLOGY

Since the mid-1970s, *Chlamydia trachomatis* has been recognized as the most common cause of NGU; *C. trachomatis* has typically been isolated in 30 to 40% of cases of NGU, although the prevalence of *C. trachomatis* in men with NGU may now be declining,²⁹ and chlamydial infection is less common in older men with NGU than in younger ones. In areas of the United States where the prevalence of *C. trachomatis* has declined in recent years, most patients with symptomatic urethritis have no evidence of either gonorrhea or chlamydial infection.³⁰ Other established causes of NGU include *Trichomonas vaginalis*, HSV-2, and, in men who engage in insertive anal intercourse, enteric pathogens. Approximately one third of men with primary genital herpes have dysuria and a urethral discharge. *T. vaginalis* is a more common cause of NGU in older men. However,

Table 1 Recommended STD Screening⁷

Population	Screening Measures
All men and women	Retest all patients diagnosed with gonorrhea or <i>Chlamydia</i> infection 10–18 wk after initial treatment
Women Sexually active, age ≤ 24 yr Age > 24 yr with a new sexual partner or multiple sexual partners	Annual chlamydial screening
Pregnant women	Test for <i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> , hepatitis B virus infection, and syphilis; offer HIV testing and counseling
	Test for bacterial vaginosis in women at high risk (e.g., those with a history of preterm delivery)
	Perform Papanicolaou smear if none was performed in the past year
Men who have sex with men (MSM)*	Perform the following at least annually: serologic testing for HIV and syphilis
	Rectal culture for gonorrhea and chlamydial infection
	Pharyngeal culture for gonorrhea
	Consider serologic testing for HSV-2, particularly in HIV-negative MSM
	Serologic testing for hepatitis A and B antibodies [†]

HSV-2 = herpes simplex virus type 2; STD = sexually transmitted disease.

*Screening guidelines apply to both HIV-positive and HIV-negative MSM. HIV and hepatitis testing should be performed for patients of unknown status. Although nucleic acid amplification tests may be helpful for the detection of rectal and oropharyngeal infections caused by *C. trachomatis* and *N. gonorrhoeae*, the test is currently not Food and Drug Administration (FDA) approved for this indication. Because HSV-2 increases the risk of HIV acquisition, HSV-2 screening should be considered to aid in HIV risk assessment and counseling. More frequent screening should be considered for those at highest risk of STD.

[†]Vaccinate for hepatitis A and B if negative.

HSV and *Trichomonas* combined are probably responsible for fewer than 10% of all cases of NGU. *Ureaplasma urealyticum* and *Mycoplasma genitalium* have been associated with NGU in case-control studies and can now be detected by polymerase chain reaction (PCR) assay.^{31,32}

DIAGNOSIS

Clinical Manifestations

Clinical manifestations of urethritis include urethral discharge, dysuria, and itching at the distal urethra. Inguinal adenopathy is unusual. Likewise, fever, chills, perineal pain, scrotal mass, genital pain, and other urinary symptoms (e.g., hematuria, frequency, hesitancy, nocturia, or urgency) are unusual and should prompt consideration of alternative diagnoses, such as urinary tract infection (UTI), epididymitis, orchitis, or prostatitis. Although gonorrhea is generally associated with a more abrupt onset of symptoms and a more copious and purulent discharge than NGU, these distinctions are not reliable.

Asymptomatic and subclinical gonococcal and chlamydial urethral infections probably play an important role in sustaining endemic levels of these STDs, but their incidence is uncertain. A prospective study of gonococcal urethritis found that only 2% of infections remained asymptomatic in the 14 days after acquisition.³³ However, cross-sectional studies have demonstrated that asymptomatic infection is common among the sexual partners of infected women³⁴ and, at least in some parts of the United States that have a high prevalence of gonorrhea, in the general population of young adults.³⁵ Prospective data on the frequency of asymptomatic chlamydial urethritis are not available, but as with gonorrhea, cross-sectional studies have demonstrated

that asymptomatic or subclinical chlamydial urethritis is common.^{35,36}

Physical Examination

Objective evidence of urethral inflammation should be sought in men presenting with dysuria or urethral discharge. Physical examination should include a genital examination, preferably conducted several hours after the patient last urinated; the examination should include a search for purulent or mucopurulent discharge. If no discharge is observed, the examiner should strip the urethra from the base of the penis to the urethral meatus to elicit a discharge.

Laboratory Tests

A urethral Gram stain should be performed on all men with symptoms of urethritis, even those with no discharge evident on physical examination. Urethral specimens for Gram stain are obtained by inserting a thin calcium alginate-tipped swab 3 to 4 cm into the urethra and then rolling the swab over a glass slide. A diagnosis of urethritis is established by the presence of five or more polymorphonuclear neutrophils (PMNs) per high power or oil-immersion field. Alternatively, the diagnosis can be made through use of a centrifuged 10 to 15 mL first-void urine specimen; the diagnosis is established by the finding of 10 or more PMNs per high power field on at least one of five randomly selected fields. A positive urine leukocyte esterase test is also sufficient for establishing the diagnosis. The probability of gonorrhea has been shown to be 94.8% with the finding of gram-negative intracellular diplococci (GND); the absence of GND from smears of the same men is associated with a 92.6% probability that they have NGU rather than gonorrhea.³⁷ The presence of GND establishes the diagnosis of gonorrhea [see Figure 1]. The Gram stain should be

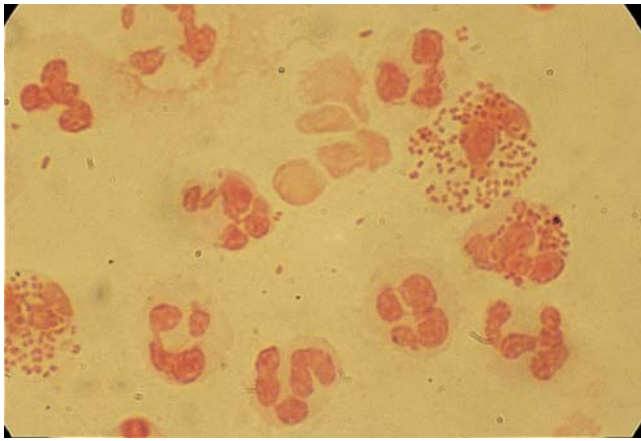


Figure 1 This figure shows a Gram stain of a urethral discharge from a man with gonorrhea. The gram-negative intracellular diplococci are *Neisseria gonorrhoeae* organisms.

considered equivocal if only extracellular organisms are seen. Regardless of Gram stain findings, specific microbiologic testing should be performed for *N. gonorrhoeae* and *C. trachomatis*.

Because it provides data on antimicrobial susceptibility, culture is recommended for male patients suspected of having gonorrhea, either alone or in combination with commercially available nucleic acid amplification tests (NAATs).³⁸

NAATs of urethral specimens or free catch urine (e.g., ligase chain reaction [LCR], PCR, transcription-mediated amplification [TMA], and strand displacement amplification [SDA]) have sensitivities comparable or superior to that of culture and are recommended for detection of reproductive tract infections caused by *C. trachomatis* and *N. gonorrhoeae* infections. Although typically more costly, these assays offer the advantage of testing without urethral swabs. In low-prevalence populations, positive NAAT results may require confirmatory testing.³⁹

TREATMENT

Initial Management

Patients with evidence of gonococcal infection on urethral Gram stain should be treated for gonorrhea. Recommended regimens include single doses of the following agents: (1) cefixime, 400 mg orally; (2) ceftriaxone, 125 mg intramuscularly; (3) ciprofloxacin, 500 mg orally; (4) ofloxacin, 400 mg orally; and (5) levofloxacin, 250 mg orally. Quinolone-resistant *N. gonorrhoeae* has recently emerged as a problem in Asia, the Pacific Islands, and, most recently, California. Consequently, quinolones are no longer recommended for the empirical treatment of gonorrhea in persons in these areas or in their contacts. Because of the high chlamydial coinfection rate, all patients with gonorrhea should also be treated for *Chlamydia*, unless that diagnosis has been microbiologically excluded. Treatment for presumptive chlamydial infection in men with NGU is with azithromycin in a single 1 g oral dose or doxycycline, 100 mg orally twice a day for 7 days.

Treatment of Recurrent or Persistent Urethritis

Although recognition of the pathogenic role of *C. trachomatis* has reduced a major cause of persistent or recurrent urethral symptoms after treatment for gonococcal urethritis, such symptoms continue to affect a minority of patients. Management should include questions regarding adherence to medical therapy and partner treatment, a urethral Gram stain to document evidence of urethral inflammation, and repeat testing for gonorrhea and chlamydial infection. Consideration should be given to possible trichomonal or herpes infection. Erythromycin, 500 mg four times a day for 7 days, with or without a single 2 g dose of metronidazole, is the recommended empirical treatment in patients who are believed to have adhered to their initial regimen and who have not been reexposed to gonorrhea or chlamydial infection.⁷

Lower Genital Tract Infections in Women

Women with STDs involving the lower genital tract may present with dysuria, urethritis or vulvovaginitis, and abnormal or altered vaginal discharge. The initial evaluation of women with these complaints seeks to differentiate urethritis, cystitis, vulvovaginitis, and cervicitis and to identify women with upper genitourinary tract infections (e.g., pyelonephritis or salpingitis). Subsequent microbiologic testing and treatment are guided by this evaluation.

SYNDROMES CAUSING DYSURIA AND URETHRITIS

STDs that can cause dysuria in women include vulvitis resulting from candidal infection and genital herpes and urethritis caused by *C. trachomatis* or *N. gonorrhoeae*. Dysuria and sterile pyuria (the presence of leukocytes and the absence of more than 102 organisms/mL of conventional urinary pathogens in a midstream urine specimen) in a woman are consistent with a diagnosis of urethral infection.⁴⁰ Other factors suggesting urethral infection include the absence of other symptoms and signs typical of UTI; risk factors or risk markers for chlamydial infection (young age, new or multiple sexual partners, failure to consistently use condoms, African-American race); symptoms lasting 7 days or longer; purulent vaginal discharge; pelvic pain or tenderness; and evidence of MPC.

Women presenting with a syndrome of dysuria and sterile pyuria should be tested for gonorrhea and chlamydial infection. Because HSV-2 can cause urethritis in women, particularly in women with primary HSV infection, the possibility of genital herpes should also be considered. HSV or candidal vulvitis typically causes external, as opposed to internal, dysuria, which occurs when urine comes in contact with the introitus or labia. Women with these infections typically have vulvar irritation or lesions, vaginal discharge, or a history of either HSV or candidal vaginitis.

In the differential diagnosis of dysuria in women, particular attention should be given to bacterial UTI, which is the most common cause of dysuria. Symptoms, signs, and laboratory findings that support the diagnosis of bacterial cystitis include urinary frequency or urgency, a history of UTI, duration of symptoms of less than 4 days, gross or microscopic hematuria, the patient's belief that she has a

UTI, suprapubic tenderness, a positive urine nitrite test, and evidence of typical urinary tract pathogens on Gram stain or urine culture.^{41–43} Fever or flank pain in a woman with dysuria and other findings consistent with UTI suggests pyelonephritis. Vaginal discharge or irritation is not typical of UTI.

Diagnostic testing for gonococcal and chlamydial urethritis in women should be based on specific tests [see Laboratory Tests, *above*]. In women with no evidence of PID, treatment is identical to that for men [see Treatment, *above*].

SYNDROMES CAUSING VULVOVAGINITIS AND VAGINAL DISCHARGE

Abnormal vaginal discharge is one of the most common reasons for women to seek medical attention. Since the 1960s, the number of women receiving care for vulvovaginal infections increased approximately threefold. Trichomonal vaginitis (TV) is the most common sexually transmitted bacterial infection in the United States, with an estimated 3 million new cases annually, and thus the most common cause of abnormal vaginal discharge.²⁶ The two other most common causes are bacterial vaginosis (BV) and vulvovaginal candidiasis (VVC) [see Table 2]. Both BV and trichomoniasis have been associated with preterm labor.^{44,45} However, to date, treatment of these infections has not definitively been shown to decrease preterm delivery.^{46–49} BV has been identified as a risk factor for PID, and both BV and trichomoniasis may increase the risk of HIV acquisition and transmission.⁵⁰ Consequently, these diagnoses have assumed new importance in HIV prevention.

Evaluation of women with vaginal complaints should include a pelvic examination and a directed laboratory evaluation. Although these infections tend to have different clinical features, a study of patients triaged and selectively treated after a telephone assessment found poor agreement between the diagnosis made by nurses and other providers and the diagnoses obtained after examination and testing.⁵¹ In addition, a study of over-the-counter antifungal therapies found that 45% of products available to women in the feminine hygiene section of stores surveyed could not be confirmed to be effective for treating infectious vaginitis; women may also be misdiagnosing themselves.⁵² These findings emphasize the need for a complete evaluation in women complaining of vaginal discharge or discomfort. Less frequent causes of vaginitis include atrophic vaginitis with secondary bacterial infection, vaginitis associated with foreign bodies or toxins, *Staphylococcus aureus* vaginitis associated with toxic-shock syndrome, group A *Streptococcus*-associated vaginitis, desquamative vaginitis (clindamycin responsive), erosive lichen planus, allergic vaginitis, vaginitis associated with autoimmune disease, and idiopathic vaginitis.⁵³

Bacterial Vaginosis

BV is the most common cause of vaginal discharge in women of reproductive age. Prevalence studies have found BV in 10 to 40% of women tested, with higher rates of infection in women tested in STD clinics and in African Americans. Douching and use of intrauterine devices (IUDs) have also been associated with BV.⁵⁴

Pathophysiology and transmission The etiology of BV is unknown. The syndrome constitutes a disturbance in normal vaginal bacterial flora characterized by a reduction in the concentration of hydrogen peroxide-producing lactobacilli⁵⁵ and increased growth of mixed bacterial flora that include *Gardnerella vaginalis*, anaerobes, and *Mycoplasma hominis*. There is evidence that BV can be transmitted sexually. This evidence includes the following: there is a high prevalence of BV in patients being treated at STD clinics; there are high rates of concordant BV among lesbian sexual partners⁵⁶; longitudinal studies have associated BV with having higher numbers of sexual partners and with having new sexual partners⁵⁷; and BV can even be found in virgins.⁵⁸ Evidence against sexual transmission includes the lack of benefit from treating sexual partners^{59,60} and inconsistent associations with levels of sexual activity.

Diagnosis Physical examination of women with BV typically reveals a homogeneous, white, uniformly adherent vaginal discharge.⁵⁴ The Amsel criteria for diagnosis of BV include the following: (1) presence of a homogeneous, thin vaginal discharge; (2) vaginal pH greater than 4.5; (3) clue cells (bacteria attached to vaginal epithelial cells on wet mount); and (4) presence of an amine (fishy) odor when vaginal fluid is mixed with 10% potassium hydroxide (KOH).^{58,61,62} The presence of three of the four criteria establishes the diagnosis [see Table 3].

Treatment BV is treated with metronidazole. A meta-analysis found higher cure rates with a dosage of 1 g a day for 7 days than with a single 2 g dose (82% versus 73%).⁵⁴ The latest therapeutic agent being studied is tinidazole.⁶³ Intravaginal metronidazole and intravaginal clindamycin offer efficacy comparable to 7-day courses of metronidazole, with fewer side effects, but are not effective in the treatment of trichomoniasis and are typically more costly. Recurrence of BV is common, occurring in 50 to 70% of cases. Multiple randomized trials have failed to demonstrate any benefit from treating male partners.^{59,60}

Trichomoniasis

T. vaginalis is a sexually transmitted protozoan. In the United States, the number of women seeking care for TV declined by over 50% from 1966 to the mid-1980s; currently, there are an estimated 3 million new cases annually.²⁶ A cross-sectional study of 13,816 pregnant women in the United States found TV in 13%; the vast majority of those infections were subclinical or asymptomatic. Risk factors for TV included African-American ethnicity, cigarette smoking, unmarried status, and lower educational level.⁶² Untreated infections in women may last undetected for 3 months or longer.⁶⁴

Diagnosis Clinical manifestations of trichomonal infection include yellow vaginal discharge and vulvar itching. Neither is highly sensitive or specific. On physical examination, signs associated with *Trichomonas* infection include frothy or purulent vaginal discharge, which is sometimes profuse; vulvar or vaginal erythema; and cervical mucopus.^{65,66} All of these signs have far greater specificity than sensitivity. The finding of colpitis macularis—punctate

Table 2 Clinical Features and Management of Vulvovaginitis

Feature	Normal Vaginal Examination	Vulvovaginal Candidiasis	Trichomonal Vaginitis	Bacterial Vaginosis
Etiology	Uninfected; lactobacilli predominate	<i>Candida albicans</i> most common; candidiasis caused by species other than <i>C. albicans</i> may be increasing	<i>Trichomonas vaginalis</i>	Loss of normal vaginal lactobacilli; associated with <i>Gardnerella vaginalis</i> ; increased anaerobic bacteria and mycoplasmas
Symptoms	None	Abnormal vaginal discharge, external dysuria, vulvar itching, pain and/or irritation	Yellow vaginal discharge, external dysuria, vulvar itching	Increased, abnormal, or malodorous vaginal discharge
Discharge				
Amount	Variable	Scant	Profuse	Moderate
Color	Clear or white	White	Yellow	White or gray
Consistency	Nonhomogeneous, patchy (flocular)	Clumped; adherent plaques	Homogeneous or frothy	Adherent, homogeneous discharge that uniformly coats vagina
Inflammatory findings	None	Vulvar erythema, edema, or fissure; erythema of vaginal epithelium; introitus	Erythema of vaginal and vulvar epithelium; colpitis macularis	None
pH of vaginal fluid*	Usually ≤ 4.5	Usually ≤ 4.5	Usually > 4.5	Usually > 4.5
Amine (fishy) odor with 10% KOH	None	None	May be present	May be present
Microscopy	Normal epithelial cells; lactobacilli predominate	Leukocytes, epithelial cells; mycelia or pseudomycelia [†] (50–85% of cases)	Leukocytes; trichomonads seen in 50–70% of culture-positive cases	Clue cells (81–94% of cases); few leukocytes; lactobacilli outnumbered by mixed flora
Recommended treatment	—	Intravaginal imidazole (butoconazole, clotrimazole, miconazole, terconazole, tioconazole) for 3–7 days; fluconazole, 150 mg p.o. (single dose)	Metronidazole, 2 g p.o. (single dose); metronidazole, 500 mg p.o., b.i.d., for 7 days	Metronidazole, 500 mg p.o., b.i.d., for 7 days; metronidazole gel, 0.75%, 5 g intravaginally each night for 5 nights; clindamycin cream 2%, 5 g intravaginally each night for 7 days
Sexual partner treatment	—	None if asymptomatic; topical treatment if candidal dermatitis of the penis or balanitis is detected	Metronidazole, 2 g orally (single dose)	None

KOH = potassium hydroxide.

*pH determination is not useful if blood is present.

[†]To detect fungal elements, vaginal fluid is digested with 10% KOH before microscopic examination; to examine for other features, fluid is mixed (1:1) with normal saline. Culture may be necessary if microscopy results are negative and the suspicion of *Candida* is high.

cervical hemorrhages and ulcers, sometimes referred to as strawberry cervix—has a specificity of 99% for TV but is seen in fewer than 5% of patients on unaided physical examination; colpitis macularis is much more readily visible on colposcopy.⁶⁵ In expert hands, a finding of motile *Trichomonas* on wet-mount examination has a sensitivity of 50 to 70%, although in clinical practice, wet-mount examination is usually considerably less sensitive. Culture on Diamond medium is the traditional diagnostic gold standard, but this technique is not available in most practice settings. The sensitivity of InPouch, a relatively simple and inexpensive culture method, is comparable to that of Diamond medium

and superior to that of wet mount.⁶⁷ PCR has been successfully used in research settings, but no NAAT is commercially available at present. Antigen detection tests are also under investigation.

Treatment A single 2 g dose of metronidazole is the treatment of choice for TV. Reported cure rates are 82 to 88%.⁶⁶ Sexual partners should be treated concurrently, and couples should be advised to abstain from sex for 1 week after treatment. Topical metronidazole is not effective.⁶⁸ Resistance to metronidazole occurs infrequently, and most cases respond to prolonged courses of metronidazole

Table 3 Amsel Criteria for the Diagnosis of Bacterial Vaginosis^{58,62}

Criterion	Sensitivity (%)	Specificity (%)
Homogeneous, thin vaginal discharge	52–65	71–97
Vaginal pH > 4.5	92–97	53–62
Clue cells on vaginal wet mount	81–94	94–98
Amine odor when vaginal fluid is mixed with 10% potassium hydroxide (KOH)	43–84	98–99

The presence of three of these four criteria establishes the diagnosis of bacterial vaginosis.

therapy. Some authors have reported successful treatment of metronidazole-resistant cases using either tinidazole or paromomycin cream.⁶⁹

Vulvovaginal Candidiasis

Because VVC is not a reportable infection, only limited epidemiologic data are available. In the United States, a study of female university students found that over half experienced at least one episode of VVC by 25 years of age,⁷⁰ and 6.5% of women who participated in a national random digit-dialing survey reported that a health care provider had told them they had candidal vaginitis at least once in the preceding 2 months.⁷¹ Higher rates of VVC have been observed in African Americans and in users of oral contraceptives, vaginal sponges, or IUDs.⁷² Although VVC is not clearly identified as an STD, it has been associated with the onset of sexual activity in young women and with cunnilingus.^{70,72} Other predisposing factors include recent use of antibiotics, diabetes mellitus, pregnancy, and immunodeficiency, including that from HIV infection.

Diagnosis Vulvovaginal pruritus is generally the most common symptom of VVC.⁷³ Other findings sometimes associated with VVC include a cottage cheese–like discharge; external dysuria; external genital burning or pain; perineal edema or erythema; and vulvar erythema, edema, and fissures.^{73,74} However, several studies have reported the absence of any signs or symptoms significantly associated with VVC.^{4,75} As a result, the diagnosis requires microscopic and, at times, microbiologic assessment. A 10% KOH preparation of fluid taken from the vagina has a sensitivity of 50 to 85% in the diagnosis of VVC^{76,77}; if this test is negative but the clinical picture is consistent with VVC and there is no alternative diagnosis, culture for yeast should be performed.

Treatment Topical azoles (e.g., butoconazole, clotrimazole, miconazole, econazole, tioconazole, and terconazole) are 80 to 90% effective in treating VCC [see Table 2]. Most of these agents are available over the counter. No clear advantage favors one azole over another. Oral azoles (fluconazole or itraconazole) are comparably or slightly more effective and may be more convenient, but these agents also pose a

small risk of systemic reactions. Because there are no compelling data favoring any one agent or route of administration, patient preference should guide the choice of treatment. Immunosuppressed patients and those with candidal infections caused by a species other than *Candida albicans* may require more prolonged therapy (e.g., 14 days).

Long-term therapy is indicated for patients with recurrent VVC, which is defined as four or more episodes of VCC in a year. Approximately 5% of women with VVC experience recurrences. Treatment may require 14 days of induction therapy followed by once-weekly maintenance therapy. Patients with *Candida glabrata* VVC who do not respond to prolonged courses of azole therapy may benefit from topical boric acid (600 mg once a day for 2 weeks) or topical flucytosine.⁷⁸

Mucopurulent Cervicitis

MPC is an inflammatory process affecting the columnar epithelium and subepithelium of the endocervix and adjacent exocervix. As with NGU in men, MPC is common and has most frequently been associated with *N. gonorrhoeae* or *C. trachomatis* and, less frequently, with HSV or *T. vaginalis*. Unlike NGU, MPC typically produces no symptoms, or it may produce nonspecific symptoms, such as a yellow vaginal discharge, that often do not prompt women to seek treatment. In recent years, as the prevalence of gonorrhea and chlamydial infections has decreased in some settings, MPC with no defined microbiologic etiology has come to constitute the majority of cases.⁴ MPC is important because of its association with known infections and because patients with MPC have an elevated risk of PID and adverse pregnancy outcome.

Diagnosis Different diagnostic criteria have been used for MPC. According to current CDC guidelines, the diagnosis of MPC is made on the basis of a finding of a visible purulent or mucopurulent exudate on cervical examination or on endocervical swab. The finding of cervical mucopus is 28 to 52% sensitive and 82 to 94% specific for the presence of either *C. trachomatis* or *N. gonorrhoeae*.^{74,79,80} Some investigators use additional criteria for MPC, including a finding of from 20 to 30 PMNs per high-power field on cervical Gram stain or easily induced cervical bleeding.^{4,80} These factors have been associated with the likelihood of *C. trachomatis* or *N. gonorrhoeae* infection, but they have not consistently been included as diagnostic criteria of MPC; with regard to the use of cervical Gram stain, these findings have not consistently been useful in defining a population in need of empirical therapy.

Treatment The decision to treat MPC is based largely on the local prevalence of *C. trachomatis* or *N. gonorrhoeae* and on the patient's risk. In areas where both gonorrhea and chlamydial infection are common, empirical therapy should be directed at both pathogens. In areas where gonorrhea rates are low, treating for *Chlamydia* infection alone is reasonable. Recent evidence suggests that in areas where the prevalence of both infections is low, older patients (i.e., those older than 30 years) suspected of having MPC need not be treated until microbiologic test results are available, provided that follow-up care is ensured.⁸⁰

Pelvic Inflammatory Disease

PID is an inflammatory process involving a variable combination of endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. PID can be blood-borne (e.g., tuberculosis) or result from extension of an intra-abdominal process. At present, however, PID most often develops when bacteria ascend from the vagina or cervix into the endometrium, fallopian tubes, and pelvic peritoneum. Although the number of women seeking care for PID has declined by over 25% since the 1980s, 8% of participants in the 1995 National Survey of Family Growth, a national representative sample of women in the United States, reported a history of PID.⁸¹ Identified risk factors for PID include a previous history of PID, higher numbers of lifetime sex partners, douching, and a history of bacterial STD. In the past, IUD use was identified as a risk factor, but its importance beyond the first 30 days after insertion is now controversial; a recent case-control study found no association between the use of currently available copper IUDs and the occurrence of PID.⁸² Gynecologic procedures that disrupt the protective cervical barrier (e.g., pregnancy termination, IUD insertion, dilation and curettage, and hysterosalpingography) elevate the risk of PID and may lead to PID in the absence of classic sexually transmitted pathogens.

MICROBIOLOGY

Studies of PID conducted in the United States and Europe in the 1980s typically implicated *C. trachomatis*, *N. gonorrhoeae*, or both as a cause of PID in approximately half of cases.⁸³ Frequently, these bacteria were part of a polymicrobial infection involving diverse normal vaginal flora, including anaerobic bacteria, facultative anaerobes, and genital mycoplasmas. *M. genitalium* has been associated with endometritis and PID.⁸⁴ *Actinomyces israelii* is a cause of PID in women with IUDs.

DIAGNOSIS

The diagnosis of PID is difficult. To date, studies have been unable to identify any single clinical finding or constellation of findings that allow accurate identification of women with PID.^{85,86} Moreover, PID studies have typically enrolled only women with overt disease and, consequently, have not provided an accurate picture of the full spectrum of the clinical entity. Indeed, most cases of PID probably go undiagnosed. Approximately two thirds of women with postinfectious fallopian tube occlusion report no history of PID, although many have sought care for abdominal pain.⁸⁷ When the diagnosis is made clinically, it may not be supported by surgical findings. Only 60 to 70% of women with clinically diagnosed PID typically have laparoscopic evidence of PID.⁸⁸

In clinically detected cases, the cardinal symptom of PID is pelvic or abdominal pain. The pain is typically dull or aching. Onset can be acute or subacute and frequently occurs at the beginning of menses. Typically, patients present after having symptoms for less than 2 weeks. In a study of a data set of patients spanning 9 years, a study compared the relation between signs and symptoms and the presence of laparoscopically diagnosed PID. The variables included

abnormal vaginal discharge, fever > 38°C, vomiting, menstrual irregularity, ongoing bleeding, symptoms of urethritis, rectal temperature > 38°C, marked tenderness of pelvic organs on bimanual examination, adnexal mass, and erythrocyte sedimentation rate of 15 mm in the first hour. The study concluded that three variables significantly influenced the prediction of the presence of PID: erythrocyte sedimentation rate, fever, and adnexal tenderness. These variables correctly classified 65% of patients with laparoscopically diagnosed PID.⁸⁹

The differential diagnosis of PID includes other causes of abdominal or pelvic pain. Depending on the clinical circumstances, the physician may need to consider such disorders as appendicitis, endometriosis, bleeding corpus luteum, pelvic adhesions, gastroenteritis, and ectopic pregnancy.

Although laparoscopy has been the traditional gold standard for diagnosing PID, many women with abnormal fimbrial biopsies have normal results on laparoscopy. Moreover, some women have histologic evidence of endometritis without salpingitis,⁹⁰ which suggests that laparoscopy may be insensitive for the detection of milder cases or of PID that is restricted to the uterus.

Transvaginal ultrasonography (TVUS) should be performed when symptoms are severe, when the physical examination reveals a pelvic mass, or when the diagnosis of PID is uncertain. Studies assessing the performance of different imaging modalities in the diagnosis of PID have been small, with no single study enrolling more than 50 patients with the diagnosis.⁸⁸ A case-control study of power Doppler TVUS reported a sensitivity of 100% and a specificity of 80%,⁹¹ suggesting that it may offer advantages over conventional TVUS. In women with tubo-ovarian abscess, repeat TVUS is often indicated to assess response to therapy. Small studies of computed tomography and pelvic magnetic resonance imaging have also reported high sensitivity and specificity. Laparoscopy should be performed if appendicitis, ectopic pregnancy, or ruptured abscess is suspected; laparoscopy should also be considered in women who do not respond to antibiotics.

TREATMENT

Because the diagnosis of PID can be challenging, the sequelae of PID can be severe, and treatment is safe and inexpensive, all patients suspected of having PID should undergo treatment for PID. The CDC recommends initiating treatment of PID in all sexually active young women with adnexal tenderness or cervical motion tenderness.⁷ These criteria are likely to be sensitive, but they are also quite nonspecific.⁸⁶

Treatment for PID is directed against *C. trachomatis*, *N. gonorrhoeae*, gram-negative facultative anaerobes, vaginal anaerobes, and streptococci. Numerous regimens have been found acceptable [see Table 4]. A recent randomized trial in women with mild to moderate PID found no advantage of inpatient therapy with intravenous cefoxitin and doxycycline over outpatient therapy with a single intramuscular dose of cefoxitin and probenecid followed by oral doxycycline.⁹² Indications for hospitalization include the following: (1) inability to exclude a possible surgical emergency (e.g., appendicitis), (2) pregnancy, (3) failure to respond to oral antibiotics, (4) inability to tolerate or adhere to outpatient oral therapy, (5) tubo-ovarian abscess, and (6) inability to

Table 4 Treatment Regimens for Pelvic Inflammatory Disease

Route	Regimen
Parenteral*	Cefotetan, 2 g IV q. 12 hr or Cefoxitin, 2 g IV q. 6 hr plus Doxycycline, 100 mg p.o. or IV q. 12 hr
	Clindamycin, 900 mg IV q. 8 hr plus Gentamicin, 2 mg/kg IV or IM once, then 1.5 mg/kg IV q. 8 hr (single daily dose may be used)
	Ofloxacin, 400 mg IV q. 12 hr or Levofloxacin, 500 mg IV q.d. plus Doxycycline, 100 mg p.o. or IV q. 12 hr with or without Metronidazole, 500 mg IV q. 8 hr or Ampicillin-sulbactam, 3 g IV q. 6 hr
	Ofloxacin, 400 mg p.o., b.i.d. or Levofloxacin, 500 mg IV q.d. for 14 days with or without Metronidazole, 500 mg p.o., b.i.d., for 14 days
	Ceftriaxone, 250 mg IM once or Cefoxitin, 2 g IM once with probenecid, 1 g p.o. plus Doxycycline, 100 mg b.i.d. for 14 days with or without Metronidazole, 500 mg p.o., b.i.d., for 14 days
Oral	

*Parenteral therapy can be discontinued after the patient improves clinically, but doxycycline should be continued for 14 days.

reliably ensure follow-up. Patients should show significant improvement within 3 days after starting therapy. Those receiving oral therapy should be reevaluated within 72 hours. Treatment should include efforts to ensure that sexual partners also receive therapy. In addition, patients with *Chlamydia* or *N. gonorrhoeae* infections should be rescreened for those infections 10 to 18 weeks after treatment.

COMPLICATIONS

Although the vast majority of women with PID in developed nations recover fully, long-term sequelae are common; these sequelae include tubal infertility, ectopic pregnancy, and chronic pelvic pain. In the largest study of PID sequelae performed to date, Swedish investigators performed laparoscopy on 1,730 women with suspected PID and then followed them for a mean of 6.9 years. After a single episode of PID, 8% of patients suffered tubal infertility, compared with 1% of control subjects in whom there was no laparoscopic evidence of PID. Of PID patients who subsequently became pregnant, 10% had an ectopic pregnancy, compared with 1% of women without PID. Similarly, pelvic pain lasting longer than 6 months occurred in 17% of women with PID but in only 2% of control subjects.⁹³ Recurrent episodes of PID multiplied the risk of sequelae [see Figure 2], as did more severe PID and longer duration of symptoms before treatment.

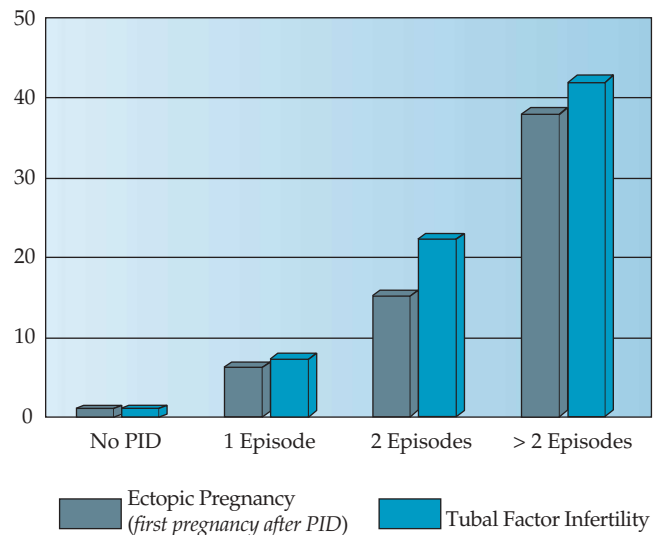


Figure 2 Proportion of women experiencing an ectopic pregnancy or tubal infertility by number of episodes of pelvic inflammatory disease (PID) among 1,282 patients with PID and 448 control subjects.^{83,93}

Genital Ulcer Disease

Genital ulcers are a frequent presentation of STDs. Epidemiologic studies, as well as studies measuring HIV shedding, suggest that GUD increases the risk of both HIV acquisition and HIV transmission.⁹⁴ As a result, the prevention and treatment of GUD are a high public health priority.

ETIOLOGY

Herpes, syphilis, and chancroid are the major causes of GUD. Less common causes of GUD include LGV (infection with L serotypes of *C. trachomatis*), donovanosis (infection with *Calymmatobacterium granulomatis*), superinfection of ectoparasitic infections, trauma, neoplasm, Behçet syndrome, Reiter syndrome, and fixed drug eruptions (e.g., from doxycycline or sulfonamides).

Herpes is the most common cause of GUD in developed nations. In the United States in 2000, over 2 million people sought care for genital herpes. In contrast, 5,979 cases of primary and secondary syphilis and 82 cases of chancroid were reported to the CDC.²⁶ Many patients with genital ulcers have concurrent HSV, syphilis, gonorrhea, chlamydia, and chancroid.⁹⁵

Traditionally, chancroid and syphilis have been the most common cause of genital ulcers in most developing nations. However, recent studies undertaken in sub-Saharan Africa have documented the increasing importance of herpes as a cause of GUD, particularly in areas where HIV is highly prevalent.⁹⁶

DIAGNOSIS

Clinical Manifestations

When examining patients with genital ulcers, clinicians should note the number and depth of lesions; the presence

of vesicles, induration, necrotic material on the ulcer bed, or an undermined ulcer border (i.e., the ulcer invades beneath the superficial edges); the presence or absence of pain; and any associated adenopathy [see Table 5]. Although physical findings can be helpful, different GUD etiologies cannot be reliably distinguished by physical examination alone.⁹⁷

Laboratory Tests

Because physical findings are unreliable, clinical assessment should be supported by laboratory evaluation. The laboratory evaluation of GUD typically concentrates on herpes and syphilis. Chancroid, donovanosis, or LGV should be considered if the patient lives in or has traveled to an area where one of those infections is common or if the physical findings are highly suggestive of one of those infections.

When possible, laboratory evaluation should include dark-field microscopy, serologic testing for syphilis (e.g., rapid plasma reagin [RPR] or Venereal Disease Research Laboratory [VDRL] and fluorescent treponemal antibody [FTA] or microhemagglutination assay for antibody to *T. pallidum*), and culture for herpes. If available, RPR should be performed. Dark-field microscopy is 70 to 95% sensitive in detecting treponemes, but sensitivity is highly dependent on the expertise of the technician. Culture should seek to distinguish between HSV-1 and HSV-2 because the former typically produces a less severe infection with fewer recurrences. This is particularly important in light of recent data that suggest that HSV-1 is an increasingly common cause of genital herpes.⁹⁸ If the initial evaluation does not establish a cause of genital ulcers and the clinician's suspicion for chancroid, LGV, or donovanosis remains low, further diagnostic efforts should focus on ruling out genital herpes. Several type-specific serologic tests that target the HSV glycoprotein G-2 (gG-2) are now available.⁹⁹ Patients who have no serologic evidence of HSV-2 may have primary infections. Only limited data are available on how soon seroconversion can be detected by commercially available type-specific tests, but the median time from exposure to seroconversion appears to be 2 to 3 weeks. Patients with a clinical syndrome consistent with genital herpes who test negative for HSV-2 should be retested after 6 to 12 weeks if an intervening recurrence of genital ulcers does not establish the diagnosis of HSV infection and the clinical suspicion for genital herpes is high. Older HSV serologic tests are neither sensitive nor specific and should not be used. Clinicians should be aware that type-specific serologic tests have not been studied extensively for HSV-2 screening. Given the imperfect specificity of these tests, it is likely that widespread testing in populations in which the prevalence of HSV-2 is low will result in large numbers of false positive test results. Because of poor specificity, a positive HSV-2 serologic test result in a patient without signs or symptoms of genital herpes or definite exposure to HSV-2 should be interpreted with caution.

TREATMENT

Treatment of patients with genital ulcers is usually empirical [see Table 6]. If patients have physical findings suggestive of syphilis, are residents of or recent travelers to areas where syphilis remains common, or are members of groups at high risk for syphilis (e.g., MSM, as well as commercial sex workers or their clients), treatment should

include benzathine penicillin G, 2.4 million units intramuscularly, and a regimen for genital herpes [see Table 7]. If the suspicion for syphilis is low and follow-up can be ensured, initial empirical treatment can focus on genital herpes alone. The treatment and follow-up of patients with genital herpes and syphilis are discussed in other subsections.

Patients with genital herpes should be counseled about the recurrent nature of the infection and advised that subclinical viral shedding is common. The median recurrence rate in the first year after HSV-2 acquisition is 0.33 recurrences monthly.¹⁰⁰ During the first 6 months after HSV-2 acquisition, the virus can be isolated by culture on 6% of days and by PCR on 20 to 35% of days.¹⁰¹ It is not known to what extent HSV can be transmitted by patients whose cultures are negative and whose PCR results are positive. The American Social Health Association Web site (<http://www.ashstd.org>) is an excellent source of information on STD in general and genital herpes in particular and has information on support services for persons with genital herpes.

STDs in Men Who Have Sex with Men and Anorectal STDs in Women

Although surveillance data on STDs in MSM are limited, cases of gonorrhea and syphilis in MSM in selected cities in the United States declined by more than 10-fold in the decade following the first recognition of AIDS.¹⁰² More recently, numerous cities in the United States and Europe have reported rising rates of STDs in MSM.^{28,103} Limited data suggest that HIV transmission may also be increasing.¹ Because STDs can enhance HIV transmission, the control of STDs in MSM is a public health priority. Moreover, an STD can be a sentinel event, alerting the clinician to a patient's risk of acquiring HIV infection or transmitting it to others.

GENERAL CONSIDERATIONS IN MSM

Several aspects of the care of MSM merit consideration. First, it is imperative that clinicians adopt a nonjudgmental, direct approach when discussing sexual behavior. In addition to the questions typically included in a sexual history, clinicians should ask patients about the HIV status of their sexual partners and about their anal sexual exposure. The latter can be determined by asking, "Are you a top, a bottom, or both a top and a bottom?" The term top refers to a man who practices insertive anal sex; a bottom practices receptive anal sex.

Second, the spectrum of STD is wider in MSM than in heterosexuals. Several pathogens that are rarely sexually transmitted among heterosexuals are relatively common causes of STD in MSM. These include hepatitis A virus, *Shigella* species, *Salmonella* species, *Campylobacter* species, *Giardia lamblia*, and *Entamoeba histolytica*. *Strongyloides stercoralis* and *Enterobius vermicularis* are occasionally transmitted sexually in MSM.

Third, the anus is a more common sexual organ for MSM than it is for heterosexuals. Consequently, STD should figure prominently in the differential diagnosis of MSM who present with anorectal symptoms, and rectal screening should be part of standard STD screening in MSM.²² Finally,

Table 5 Clinical Features and Laboratory Diagnosis of Genital Ulcers

Disease	Etiology	Incubation Period	Number of Lesions	Primary Lesion Type	Ulcer Diameter	Ulcer Characteristics	Pain or Tenderness	Lymphadenopathy	Laboratory Diagnosis
Syphilis	<i>Treponema pallidum</i>	9–90 days	Usually one	Papule	5–15 mm	Superficial or deep; sharply demarcated; indurated; nonvascular, purulent base	Uncommon	Firm, nontender, bilateral	Dark-field microscopy, RPR/VDRL and FTA, MHA-TP
Herpes	HSV-1 or -2	2–7 days	Multiple, may coalesce	Vesicle	1–2 mm	Superficial; erythematous edges, no induration	Frequently tender	Firm, tender, small; often bilateral with first episode	DFA, culture, serology
Chancroid	<i>Haemophilus ducreyi</i>	1–14 days	Multiple, may coalesce	Pustule	Variable	Deep; irregular, undermined edges; purulent base bleeds easily	Usually tender	Tender, may be fluctuant, loculated; usually unilateral	Culture of ulcer base,* NAAT (e.g., PCR, LCR, TMA, SDA)
LGV	L serotypes of <i>Chlamydia trachomatis</i>	3 days to 6 wk	Usually one	Papule, pustule, or vesicle	2–10 cm	Very rarely seen because of rapid healing; can be superficial, deep, elevated, round, or oval	Variable	Tender, may suppurate or form sinus tracts; loculated, usually unilateral; more common in men than women	Culture, PCR, micro-immunofluorescent antibody
Donovanosis	<i>Calymmatobacterium granulomatis</i>	1–4 wk (up to 6 mo)	Variable	Papule	Variable	Extensive, indolent ulcer with granulation tissue; elevated, rolled irregular edges on raised ulcer; beefy-red vascular base bleeds easily [†]	Uncommon	None; pseudobuboes	Giemsa or Wright stain of tissue smear

DFA = direct fluorescent antibody; FTA = fluorescent treponemal antibody; HSV = herpes simplex virus; LGV = lymphogranuloma venereum; LCR = ligase chain reaction; MHA-TP = microhemagglutination assay-*Treponema pallidum*; NAAT = nucleic acid amplification test; PCR = polymerase chain reaction; RPR = rapid plasma reagin; SDA = strand displacement amplification; TMA = transcription-mediated amplification; VDRL = Venereal Disease Research Laboratory.

*Culture of material from bubo seldom positive.

[†]Less common variants can be hypertrophic, necrotic, or sclerotic.

although there are no guidelines for regular STD screening of heterosexual men, the CDC currently recommends annual STD screening for MSM [see Table 1].⁷

PROCTITIS, PROCTOCOLITIS, AND ENTERITIS

Although anorectal STD occurs in both men and heterosexual women, anal STD syndromes are more common in

MSM. The symptoms of anorectal infection vary, depending on the level and extent of anatomic involvement and on the microbiologic etiology.¹⁰⁴ Proctitis is limited to the rectum. It results from direct inoculation of pathogens through anal sex and presents as some combination of rectal pain, constipation, hematochezia, tenesmus, and mucopurulent rectal discharge. Sexually transmitted proctitis is caused by

Disease	Regimen
Syphilis	Benzathine penicillin G, 2.4 million U IM*
Chancroid	Azithromycin, 1 g p.o. once or Ceftriaxone, 250 mg IM once or Ciprofloxacin, 500 mg p.o., b.i.d., for 3 days
Lymphogranuloma venereum	Doxycycline, 100 mg p.o., b.i.d., for 21 days
Donovanosis	Doxycycline, 100 mg p.o. for at least 3 wk or until lesion is healed or Trimethoprim-sulfamethoxazole, double strength (800 mg/160 mg), one tablet p.o., b.i.d., for at least 3 wk or until lesion is healed
Herpes	See Table 7

Treatment should always include evaluation and treatment of sexual partners.
*For primary or secondary syphilis.

gonorrhea, chlamydial infection (non-LGV), syphilis, or HSV. In proctocolitis, the inflammatory process extends to the colon. As a result, in addition to the symptoms of proctitis, patients may complain of diarrhea, abdominal pain, and bloating or nausea. Most cases of proctocolitis result from oral-genital or oral-anal sex (anilingus, or so-called rimming) and are caused by *Shigella*, *Salmonella*, or *Campylobacter* species; *E. histolytica*; or LGV serovars of *C. trachomatis*. *G. lamblia* infection involves the small bowel alone (enteritis) and typically presents as diarrhea, abdominal pain, and bloating or nausea in the absence of rectal symptoms. The differential diagnosis in patients presenting with symptoms of colitis or proctocolitis should include *Clostridium difficile* infection and inflammatory bowel disease. In persons with HIV infection and CD4⁺ T cell counts less than 50/ μ L, cytomegalovirus infection is also a possibility. Depending on their level of immunosuppression, HIV-infected patients presenting with enteritis should also be

Disease	Regimen
Primary herpes	Acyclovir, 400 mg p.o., t.i.d., for 7–10 days or Valacyclovir, 1 g p.o., b.i.d., for 7–10 days or Famciclovir, 250 mg p.o., t.i.d., for 7–10 days
Recurrent herpes	Acyclovir, 800 mg p.o., b.i.d., for 5 days or Acyclovir, 800 mg p.o., t.i.d., for 2 days or Valacyclovir, 1 g p.o., q.d., for 5 days or Valacyclovir, 500 mg p.o., b.i.d., for 3–5 days or Famciclovir, 125 mg p.o., t.i.d., for 5 days

evaluated for *Mycobacterium avium* complex, cryptosporidium, *Isospora belli*, *Cyclospora cayetanensis*, and *Microsporidia* organisms.

DIAGNOSIS

History and Physical Examination

Evaluation of a patient with anorectal symptoms should include questions about anal, oral-genital, and oral-anal sex and condom use. In the evaluation, an attempt should be made to differentiate symptoms of proctitis, proctocolitis, and enteritis. Physical examination should include a careful anal examination, digital rectal examination, and anoscopy directed toward finding ulcers consistent with HSV or syphilis, condylomata lata, or rectal discharge or bleeding.

Laboratory Tests

If a rectal exudate is present, a Gram stain should be performed to look for gonorrhea. The reported sensitivity of Gram stain is highly variable, and in one study, 12% of chlamydial and 5% of gonococcal infections had no Gram stain evidence of urethral inflammation. Absence of symptoms and discharge is not uncommon in chlamydial infection, and without testing, many infections will go untreated.¹⁰⁵ In men without rectal symptoms, however, anoscopically obtained rectal cultures do not appear to be more sensitive in detecting gonorrhea than those obtained by blindly inserting a swab 2 to 3 cm into the rectum.¹⁰⁶

Laboratory evaluation in patients with suspected proctitis or proctocolitis should include cultures for gonorrhea and chlamydial infection, a serologic test for syphilis, and a rapid syphilis test. Rectal ulcers or lesions should be cultured for HSV; when possible, a specimen should be obtained for dark-field evaluation. If symptoms suggest proctocolitis, stool specimens should be obtained for enteric pathogens and *E. histolytica*. Patients with recent antibiotic exposures should also be tested for *C. difficile*. Stool *Giardia* antigen testing should be performed if enteritis is suspected.

TREATMENT

In general, treatment should be directed by laboratory findings. If patients with proctitis have severe symptoms or if follow-up cannot be ensured, empirical therapy should be directed against gonorrhea and chlamydial infection. The CDC recommends treatment with ceftriaxone, 250 mg intramuscularly, and doxycycline, 100 mg a day orally for 7 days. Alternative therapies for gonorrhea (cefixime, 400 mg orally or ciprofloxacin, 500 mg orally once) and chlamydial infection (azithromycin, 1 g orally once) are probably effective but have not been studied. Clinicians should have a low threshold for adding empirical therapy for herpes to this regimen.

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