U.S. Centers for Disease Control and Prevention Guidelines for the Treatment of Sexually Transmitted Diseases: An Opportunity To Unify Clinical and Public Health Practice

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Sexually transmitted diseases (STDs) constitute an epidemic of tremendous magnitude, with an estimated 15 million persons in the United States acquiring a new STD each year. Effective clinical management of STDs is a strategic common element in efforts to prevent HIV infection and to improve reproductive and sexual health. Sexually transmitted diseases may result in severe, long-term, costly complications, including facilitation of HIV infection, tubal infertility, adverse outcomes of pregnancy, and cervical and other types of anogenital cancer. The publication of national guidelines for the management of STDs, by the U.S. Centers for Disease Control and Prevention (CDC), has been a key component of federal initiatives to improve the health of the U.S. population by preventing and controlling STDs and their sequelae. This paper presents new recommendations from the 2002 CDC Guidelines for the Treatment of Sexually Transmitted Diseases in the context of current disease trends and public health.

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Sexually transmitted diseases (STDs) have been called the "hidden epidemic" by the U.S. Institute of Medicine (1) because their scope and consequences are underrecognized by public and health care professionals. In the United States, STDs constitute an epidemic of tremendous magnitude, with an estimated 15 million persons acquiring a new STD each year (2). Reported disease rates, which grossly underestimate the true burden of infection both because most STDs are asymptomatic and because of underreporting, echo the huge scope of this epidemic. Two STDs, chlamydia and gonorrhea, are the first and second most commonly reported notifiable diseases in the United States, and they alone made up 80% of the cases of all notifiable diseases reported to the U.S. Centers for Disease Control and Prevention (CDC) in 2000 (3). As the Institute of Medicine has highlighted, reported STD rates in the United States are the highest in the industrialized world; in some U.S. communities, they rival those of developing countries.

Effective clinical management of STDs is a strategic common element in prevention of HIV infection and in efforts to improve the health of women, adolescents, and infants. This is because, if untreated, STDs often result in severe, long-term, costly complications. These diseases biologically increase risk for HIV acquisition and HIV transmission at least three- to fivefold (4). They are the leading preventable cause of involuntary infertility and potentially fatal ectopic pregnancy, and they play a major role in other adverse outcomes of pregnancy, ranging from fetal wastage to low birthweight, prematurity, and congenital infection (5). One STD, human papillomavirus infection, can cause cervical and other types of anogenital cancer (6). Indeed, because STDs are communicable diseases with far-reaching public health consequences, early detection and treatment are important, and clinicians can thus play a pivotal role in improving not only the sexual and reproductive health of individual patients but also the long-term health and health care costs of their communities.

In this paper, we examine new recommendations presented in the 2002 CDC Guidelines for the Treatment of Sexually Transmitted Diseases (7) (**Tables 1** and **2**) and discuss key, ongoing approaches to the treatment of STDs in the context of current disease trends and public health needs and opportunities. We highlight the crucial role of clinicians in reducing the severe, long-term effect of STDs on adolescents and young adults in the United States.

Prevention of STD-Related HIV Transmission

Because of compelling data linking STD acquisition and HIV transmission, early detection and appropriate treatment of STDs are considered key components of a comprehensive strategy for HIV prevention (8). Among persons with STDs, those with ulcerative STDs typically have a higher prevalence of HIV co-infection, reflecting the fact that ulcerative STDs and HIV infection have shared risk factors and strong mutually reinforcing effects: Ulcerative STDs can increase HIV transmissibility, and HIV infection can cause ulcer persistence (4).

Several recent advances have been made in the management and treatment of genital ulcer disease. In the United States, most sexually active persons with genital ulcers have genital herpes, syphilis, or chancroid (9). However, diagnosis of these conditions on the basis of medical history and physical examination is often inaccurate unless accompanied by specific diagnostic testing (10). Therefore, evaluation of all patients with genital ulcers should include a serologic test for syphilis and a diagnostic evaluation for genital herpes; in settings where chancroid is prevalent, a test for *Haemophilus ducreyi* should be done. Biopsy of ulcers may help identify the cause of unusual ulcers or ulcers that do not respond to initial therapy. Testing for

Table 1. **New Findings in the Centers for Disease Control and Prevention 2002 Guidelines for the Treatment of Sexually Transmitted Diseases**

Evaluation for chlamydial infection 3 to 4 months after primary infection
Emergence of quinolone-resistant gonorrhea and implications for treatment
Alternative treatment regimens for early syphilis and neurosyphilis in persons allergic to penicillin
Commercial availability of type-specific serologic tests for genital herpes
Treatment options for genital herpes in persons with HIV infection
Screening and treatment for bacterial vaginosis before abortion or hysterectomy to reduce postoperative infectious complications
Nucleic acid testing for human papillomavirus infection in the management of women with Papanicolaou smears showing atypical squamous cells of undetermined significance

HIV should be done in the evaluation of all patients with genital ulcer disease.

Syphilis

A readily curable, bacterial genital ulcer disease, syphilis continues to be one of the most important STDs because of its biological effect on HIV acquisition and transmission (4) and its effect on infant health. Currently, syphilis is an important problem in the southern United States and in some urban areas in other U.S. regions, and recent outbreaks have been seen among men who have sex with men (11, 12). The 2000 rate of primary and secondary syphilis, 2.2 per 100 000, is the lowest rate seen since reporting began in 1941. This historic low rate is complemented by extreme geographic clustering of disease, with half of all new cases reported from only 22 of the 3115 U.S. counties (<1%). These factors have created an unprecedented opportunity for the elimination of syphilis. This elimination would address one of our most glaring ethnic disparities in health and would result in substantial savings in health care costs. Reported cases of syphilis continue to disproportionately affect black persons, who had rates as much as 23 times greater than those in white persons in 2000 (11). The annual direct and indirect costs of syphilis in the United States are an estimated $966 million, including the cost of care for adult and congenital syphilis ($214 million) and for HIV infection attributable to syphilis ($752 million) (13). Therefore, the CDC launched a national plan to eliminate syphilis from the United States (14). Syphilis elimination has been defined at the national level as the absence of sustained transmission in the United States and at the local level as the absence of new cases within a local jurisdiction (except within 90 days of an imported index case). The national goal of the syphilis elimination program is to reduce primary and secondary syphilis to no more than 1000 cases (0.4 per 100 000 population) and to increase the percentage of syphilis-free counties to 90% by 2005. Between 1997 and 2000, the incidence of adult syphilis decreased by 30%, more than a 50% reduction in congenital syphilis was seen, and the ratio of syphilis rates in black persons to those in white persons was almost halved (11).

Long-acting preparations of penicillin remain the treatment of choice for all stages of syphilis. This treatment is supported by more than 40 years of clinical experience and a few recent clinical trials (15). Primary, secondary, and early latent syphilis are effectively treated with a single dose of 2.4 million units of benzathine penicillin G, while late latent syphilis requires three benzathine penicillin G injections given 1 week apart. Persons with HIV infection who have early syphilis (primary, secondary, or early latent) should be managed according to these standard treatment recommendations, but they may be at increased risk for neurologic complications and may have higher rates of treatment failure. Management of late latent syphilis in HIV-infected persons should include a cerebrospinal fluid examination before treatment. Assessment of therapeutic efficacy for the various stages of syphilis, regardless of HIV infection, remains complicated by lack of a well-defined, consistently observed response in the nontreponemal serologic titer. As a prospective study of early-stage syphilis recently showed (16), approximately 15% of patients did not meet standard criteria for serologic cure 12 months after appropriate treatment; this outcome was not improved by more intensive treatment regimens that provide extended, high penetration of cerebrospinal fluid. Because the relation between serologic and clinical response remains unclear in such cases and in the absence of data supporting greater effectiveness of alternative antimicrobial regimens, we continue to recommend benzathine penicillin G for early-stage syphilis, regardless of HIV status.

Despite limited data supporting the use of alternatives to penicillin in the treatment of early-stage syphilis, the treatment guidelines suggest several new alternative therapies that seem promising in nonpregnant, penicillin-allergic patients with primary or secondary syphilis. Limited clinical studies, along with biological and pharmacologic considerations, suggest that ceftriaxone should be effective for early-stage syphilis (17), but proper dose, proper duration of treatment, and efficacy have not been definitively established. Azithromycin is active against *Treponema pallidum* in in vitro models and seems to be effective in a small cohort of patients with early-stage disease, but it may prove most useful as single-dose therapy for incubating syphilis (18, 19). In the management of neurosyphilis in penicillin-allergic persons, ceftriaxone may be considered a new alternative treatment regimen. The use of any of these alternatives to penicillin in the treatment of syphilis in HIV-infected persons has not been well studied.

Genital Herpes

Genital herpes simplex virus type 2 (HSV-2) infection is the most common infectious cause of genital ulcers in the United States, with a reported seroprevalence rate of 22% in adults in the early 1990s. This rate represents a 32% increase relative to the previous decade (20). Whereas most cases of genital herpes are caused by HSV-2, genital infections with herpes simplex virus type 1 (HSV-1) are

Table 2. **Selected Recommendations from the Centers for Disease Control and Prevention 2002 Guidelines for the Treatment of Sexually Transmitted Diseases***

Condition or Need	Recommended Treatment	Alternatives
Syphilis		
Early–primary, secondary, or latent syphilis, <1 year since infection	Benzathine penicillin G (2.4 million U, IM) in a single dose	Doxycycline, 100 mg twice daily for 14 d OR oral tetracycline, 500 mg 4 times daily for 14 d
Late latent syphilis or late syphilis of unknown duration	Benzathine penicillin G, 3 doses (2.4 million U each, IM) at 1-week intervals (7.2 million U total)	Doxycycline, 100 mg twice daily for 14 d OR oral tetracycline, 500 mg 4 times daily for 28 d
Syphilis during pregnancy	Benzathine penicillin G at a dosage appropriate for the stage of syphilis	No proven alternatives
Neurosyphilis	Aqueous crystalline penicillin G (3–4 million U, IV) every 4 hours for 10 to 14 d (18 to 24 million U/d)	Procaine penicillin G (2.4 million U, IM) once daily for 10–14 d PLUS oral probenecid, 500 mg 4 times daily for 10–14 d
Genital herpes		
First clinical episode	Oral acyclovir, 400 mg 3 times daily for 7–10 d OR Oral acyclovir, 200 mg 5 times daily for 7–10 d OR Oral famciclovir, 250 mg 3 times daily for 7–10 d OR Oral valacyclovir, 1 g twice daily for 7–10 d	
Episodic recurrences	Oral acyclovir, 400 mg 3 times daily for 5 d OR Oral acyclovir, 200 mg 5 times daily for 5 d OR Oral acyclovir, 800 mg twice daily for 5 d OR Oral famciclovir, 125 mg twice daily for 5 d OR Oral valacyclovir, 500 mg twice daily for 3–5 d OR Oral valacyclovir, 1.0 g daily for 5 d	
Suppression	Oral acyclovir, 400 mg twice daily OR Oral famciclovir, 250 mg twice daily OR Oral valacyclovir, 500 mg once daily OR Oral valacyclovir, 1.0 g once daily	
Pregnancy	See complete CDC guidelines (7)	
Genital herpes and HIV infection		
Episodic recurrences	Oral acyclovir, 400 mg 3 times daily for 5–10 d OR Oral acyclovir, 200 mg 5 times daily for 5–10 d OR Oral famciclovir, 500 mg twice daily for 5–10 d OR Oral valacyclovir, 1.0 g twice daily for 5–10 d	
Suppression	Oral acyclovir, 400–800 mg 2 or 3 times daily OR Oral famciclovir, 500 mg twice daily OR Oral valacyclovir, 500 mg twice daily	
Chancroid	Oral azithromycin, 1 g in a single dose OR Ceftriaxone (250 mg, IM) in a single dose OR Oral ciprofloxacin, 500 mg twice daily for 3 d OR Oral erythromycin base, 500 mg 3 times daily for 7 d	
Chlamydia	Oral azithromycin, 1 g in a single dose Oral doxycycline, 100 mg twice daily for 7 d	Oral erythromycin base, 500 g 4 times daily for 7 d OR Oral erythromycin ethylsuccinate, 800 mg 4 times daily for 7 d OR Oral ofloxacin, 300 mg twice daily for 7 d OR Oral levofloxacin, 500 mg daily for 7 d
Chlamydia during pregnancy	Oral erythromycin base, 500 mg 4 times daily for 7 d OR Oral amoxicillin, 500 mg 3 times daily for 7 d	Oral erythromycin base, 250 mg 4 times daily for 14 d OR Oral erythromycin ethylsuccinate, 800 mg 4 times daily for 7 d OR Oral erythromycin ethylsuccinate, 400 mg 4 times daily for 14 d OR Oral azithromycin, 1 g in a single dose
Gonorrhea		
Urogenital or rectal gonorrhea†	Oral cefixime, 400 mg in a single dose OR Ceftriaxone (125 mg, IM) in a single dose OR Oral ciprofloxacin, 500 mg in a single dose OR Oral ofloxacin, 400 mg in a single dose OR Oral levofloxacin, 250 mg in a single dose PLUS Treatment for chlamydia if this infection is not ruled out	Spectinomycin, IM, 2 g in a single dose OR Single-dose cephalosporin OR Single-dose quinolone
Bacterial vaginosis		
Bacterial vaginosis in nonpregnant persons	Oral metronidazole, 500 mg twice daily for 7 d OR Metronidazole gel 0.75% (one 5-g applicator per day, intravaginally) for 5 d OR Clindamycin cream 2% (one 5-g applicator intravaginally) for 7 d every evening	Oral clindamycin, 300 mg twice daily for 7 d OR Clindamycin ovules, 100 g intravaginally for 3 d every evening OR Oral metronidazole, 2 g in a single dose
Bacterial vaginosis during pregnancy	Oral metronidazole, 250 mg 3 times daily for 7 d OR Oral clindamycin, 300 mg 3 times daily for 7 d	
Trichomoniasis	Oral metronidazole, 2 g in a single dose	Oral metronidazole, 500 mg twice daily for 7 d

* For the complete Centers for Disease Control and Prevention 2002 Guidelines for the Treatment of Sexually Transmitted Diseases, see reference 7 or www.cdc/gov/std/treatment/default.htm. CDC = Centers for Disease Control and Prevention; IM = intramuscularly; IV = intravenously.
† Quinolones should not be used for infections acquired in Asia or the Pacific, including Hawaii. The use of quinolones is probably inadvisable for the treatment of infections acquired in California and in other areas with an increased prevalence of quinolone resistance.

increasingly recognized (21). Most genital herpes infections are transmitted by persons who are unaware that they have the infection or are asymptomatic when transmission occurs. In a large population-based study (20), only 9% of HSV-2–seropositive persons reported that they had genital herpes. Because of the high proportion of unrecognized infection, the diagnosis of genital herpes should be confirmed by sensitive diagnostic tests, such as viral culture or HSV type-specific serologic tests. Accurate type-specific assays for HSV rely on the detection of antibodies to HSV-specific glycoprotein G1 and G2. Such assays became commercially available in 1999, but older assays that do not accurately distinguish HSV-1 antibody from HSV-2 antibody remain on the market. The new type-specific assays are discussed in the CDC's STD treatment guidelines and may be useful in the diagnosis of unrecognized infection and the management of sexual partners of persons with genital herpes.

Optimal management of genital herpes includes antiviral therapy and appropriate counseling on the natural history of infection, risk for sexual and perinatal transmission, and methods to prevent further transmission. Systemic antiviral drugs partially control the symptoms and signs of herpes episodes when used to treat first clinical episodes and recurrent episodes or when used as daily suppressive therapy. However, these drugs neither eradicate latent virus nor affect the risk for, frequency of, or severity of recurrences after use of the drug is discontinued. Effective antiviral regimens that provide clinical benefit for patients with genital herpes include acyclovir, valacyclovir, and famciclovir (22). Suppressive antiviral therapy reduces, but does not eliminate, subclinical viral shedding (23). Most genital herpes in HIV-infected persons responds to antiviral agents, although clinical improvement is often slower than in immunocompetent persons. Isolates from patients with persistent HSV infections unresponsive to antiviral agents should be tested for antiviral resistance. Clinically significant acyclovir resistance has not emerged among immunocompetent persons. Additional research is needed to investigate the extent to which suppressive therapy may prevent HSV transmission, regardless of HIV infection status, and HIV transmission among co-infected persons.

Chancroid

Chancroid is the ulcerative STD that has been most strongly linked to HIV transmission (4), and healing of chancroid may be slowed in persons with HIV infection. The incidence of chancroid is very low in the United States, with only 78 cases reported in 2000 (11), but this disorder is substantially underdiagnosed. Clinicians treating genital ulcers should be alert to the possibility of chancroid, which can be easily treated with single-dose azithromycin or ceftriaxone or with multiday regimens of ciprofloxacin or erythromycin. Persons with HIV infection may require longer courses of therapy than those recommended for HIV-negative persons. In addition, data are limited on the therapeutic efficacy of the recommended single-dose ceftriaxone or azithromycin regimens in HIV-infected patients, and these regimens should be used only if follow-up can be ensured.

Prevention of STD-Related Infertility

Prompt recognition and appropriate treatment of chlamydial and gonococcal infections are crucial not only in the prevention of STD-associated HIV transmission but also in the primary prevention of STD-related infertility. In women, chlamydial and gonococcal infections are often asymptomatic. Untreated, they may result in pelvic inflammatory disease; this, in turn, results in infertility, ectopic pregnancy, and chronic pelvic pain in 10% to 20% of cases (24).

Chlamydia

Chlamydia trachomatis infection is the most common bacterial STD in the United States, with an estimated 3 million cases occurring annually (2). The highest rates are in adolescent girls, and studies done in a range of venues, including secondary schools, family planning clinics, and the Job Corps, reveal prevalences of chlamydia that usually range from 4% to 15% (11, 25). Reported rates of chlamydial infection have increased dramatically over the past decade, reflecting expansion of chlamydial screening activities and the advent of a new generation of highly sensitive nucleic acid amplification tests. However, many women who are at risk for chlamydia are still not screened appropriately because of lack of awareness among some providers and limited resources available for screening.

Chlamydia screening and reporting are likely to expand further in response to the recent screening recommendations from the third U.S. Preventive Services Task Force (USPSTF) (26) and the inclusion of a chlamydia screening measure in the Health Plan Employer Data and Information Set (HEDIS), which assesses the performance of managed care organizations (27). The USPSTF, the HEDIS measure, and the STD treatment guidelines recommend routine screening of all sexually active women 25 years of age or younger and other asymptomatic women at increased risk for infection (for example, women with new or multiple sexual partners, a previous STD, or inconsistent use of barrier contraceptives). In parts of the United States where chlamydia screening and treatment programs have been widely implemented, rates of positivity for chlamydia among women attending family planning clinics have decreased by as much as two thirds (11). However, these declines have recently plateaued or reversed in most of the United States, possibly because of failure to extend screening coverage to more at-risk women and to men. This is particularly disturbing because selective chlamydia screening and treatment in women have been shown to reduce the incidence of pelvic inflammatory disease (the critical link between chlamydia and reproductive sequelae) by almost 60% (28).

Efficacious regimens for the treatment of chlamydia include azithromycin or doxycycline. Azithromycin, which can be given as single-dose, directly observed therapy, may be the more cost-effective drug in many settings, especially in persons who are unlikely to complete the 7-day doxycycline regimen (29). A test of cure is not necessary after completion of treatment with azithromycin or doxycycline unless symptoms persist or reinfection is suspected. However, because of the high incidence of new chlamydial infections in women who have had chlamydia in the preceding several months, the new CDC treatment guidelines suggest rescreening for chlamydia 3 to 4 months after treatment, especially in adolescents.

Gonorrhea

Infections due to *Neisseria gonorrhoeae*, like those resulting from *C. trachomatis*, are a major cause of cervicitis, urethritis, proctitis, and pelvic inflammatory disease. In the United States, an estimated 650 000 cases of gonorrhea occur each year (2). The reported gonorrhea rate increased approximately 10% from 1997 to 1999, after a 72% decrease from 1975 to 1997 (11). Because gonococcal infections in women are often asymptomatic, an important component of gonorrhea control continues to be the screening of women at high risk for STDs.

Several antibiotics are effective in the single-dose treatment of gonorrhea, including cefixime, ceftriaxone, ciprofloxacin, and ofloxacin (7). Concomitant therapy with a regimen effective against chlamydia is recommended because of the frequency of dual infections. Recently, quinolone-resistant gonorrhea has been reported from southeast Asia, Hawaii, and California (7, 30). Persons with gonorrhea who have recently traveled to Asia or the Pacific, Hawaii, and California and persons who have a sexual partner who has recently traveled to these areas, should receive a nonquinolone treatment regimen. However, because the national prevalence of quinolone resistance remains very low (31), the recommended treatment regimens remain appropriate for most cases of gonorrhea in the continental United States and Alaska. The prevalence of quinolone-resistant gonorrhea may increase in the next several years because of the importation of infection, and culture and susceptibility testing should be done in persons with apparent treatment failure. Spectinomycin remains an important option for treatment of gonorrhea in cephalosporin-allergic persons when quinolones cannot be used (for example, during pregnancy or in areas with a high rate of quinolone-resistant infections), although availability has recently been a concern (32).

PREVENTION OF STD-RELATED ADVERSE OUTCOMES OF PREGNANCY

Many sexually transmitted infectious agents are an important cause of adverse outcomes of pregnancy, including spontaneous abortion, stillbirth, premature birth, and congenital infection (5). Among the ulcerative STDs, syphilis remains an important cause of illness and death during pregnancy, despite the widespread availability of inexpensive serologic tests and substantial efforts to encourage routine screening through early prenatal care. Parenteral penicillin G, if provided at least 1 month before delivery, is effective in preventing maternal transmission and treating fetal infection. The appropriate dose and duration of penicillin therapy depend on the clinical stage of syphilis in the mother. Women with a history of allergy to penicillin should be desensitized and treated with penicillin; no proven alternative regimens exist for the treatment of syphilis in pregnancy.

Genital Herpes

The other genital ulcer disease frequently associated with poor pregnancy outcomes is genital herpes. The risk for neonatal HSV infection is much greater after first-episode infection than after reactivation during pregnancy (33). Primary HSV infection during late pregnancy has been associated with spontaneous abortion, premature birth, and low birthweight (34). Prevention of neonatal herpes depends on preventing herpes acquisition during late pregnancy and possible exposure of the infant to herpetic lesions during delivery. Type-specific HSV serologic screening to identify HSV-negative women has been proposed as a strategy to prevent neonatal herpes, but the feasibility and effectiveness of this approach are unknown. Seronegative women at risk for HSV infection should be counseled to avoid acquiring herpes infection in late pregnancy by refraining from genital intercourse with partners known to have or suspected to have genital herpes and from direct orogenital contact with partners known to have or suspected of having orolabial herpes. Antiviral therapy during pregnancy is recommended in women with primary HSV infection or severe herpes infection. There seems to be no increased risk for major birth defects after prenatal exposure to acyclovir. Data are insufficient to provide useful information on pregnancy outcomes with exposure to either valacyclovir or famciclovir.

Chlamydia and Gonorrhea

Cervical and vaginal infections also compromise pregnancy outcomes. Various studies (35) have inconsistently linked *C. trachomatis* infection to premature birth. However, perinatal infection can result from the acquisition of chlamydial infection during parturition. Clinical manifestations of neonatal chlamydial infection include inclusion conjunctivitis, subacute pneumonia, and rectogenital infections. Erythromycin is the recommended regimen for chlamydial infection in infants. Prenatal screening and treatment of pregnant women for chlamydia prevents chlamydial infection among neonates. Pregnant women who are younger than 25 years of age or have new or multiple sex partners should receive the highest priority for chlamydia screening.

Gonococcal infection can also affect the health of the fetus and infant in such ways as premature delivery, pre-

mature rupture of membranes, and perinatal distress (36). The most serious manifestations of *N. gonorrhoeae* infection in newborns are ophthalmia neonatorum and sepsis, including arthritis and meningitis. Although *N. gonorrhoeae* is a less frequent cause of ophthalmia neonatorum in the United States than *C. trachomatis* and nonsexually transmitted agents are, this infection is especially important because it may result in perforation of the globe of the eye and blindness. Instillation of a prophylactic agent (silver nitrate, erythromycin, or tetracycline ointments) into the eyes of all newborn infants is recommended to prevent gonococcal ophthalmia neonatorum. Diagnosing and treating gonococcal infection in pregnant women are the best ways to prevent neonatal gonococcal disease.

Bacterial Vaginosis

Bacterial vaginosis, a sexually associated infection, has also been associated with adverse pregnancy outcomes, including chorioamnionitis, premature rupture of membranes, premature birth, and postpartum endometritis (37). Although no national surveillance data are available, bacterial vaginosis is probably the most prevalent infectious cause of abnormal vaginal discharge (38). The principal goal of therapy has been to relieve vaginal symptoms, which can be accomplished with oral metronidazole, clindamycin cream, or metronidazole gel. Treatment trials show that the oral and vaginal metronidazole regimens are similarly efficacious and seem to be more effective than clindamycin cream (7). However, reported cure rates for all regimens fall short of cure rates for most other reproductive tract infections. Studies are now under way to evaluate the efficacy of vaginal lactobacilli suppositories, in addition to oral metronidazole, for initial treatment and prevention of recurrent infection. Several studies suggest that treatment of bacterial vaginosis in pregnant women with a history of preterm birth may reduce subsequent risk for prematurity (39, 40). No randomized trial has shown a reduction in adverse outcomes of pregnancy among asymptomatic women without a history of preterm birth. Additional studies are under way to clarify this difficult issue. Current evidence does not support universal screening for bacterial vaginosis in pregnancy (41).

Trichomoniasis

Vaginal trichomoniasis has been associated with adverse pregnancy outcomes, but limited data show that treatment of asymptomatic infection during pregnancy lessens the association (42). Metronidazole remains the only recommended treatment for trichomoniasis. Metronidazole use during pregnancy has not been shown to have a consistent association with teratogenic or mutagenic effects in the infant. Infections with strains that show diminished susceptibility to metronidazole can occur. Most nonpregnant women respond to a higher metronidazole dose and extended therapy. No published data on the use of these enhanced metronidazole regimens in pregnant women exist, and pregnant women should be managed in consultation with an expert in infectious diseases.

Prevention of STD-Related Cancer

It is well established that persistent infection with human papillomavirus (HPV) plays a central role in the pathogenesis of most types of squamous-cell cancer of the cervix, vagina, vulva, anus, and penis. Recent estimates of the cost of treating HPV and cervical cancer exceed $4.5 billion; this is more than the cost of any other single STD with the exception of HIV infection (1). Most invasive types of anogenital squamous-cell cancer of the genital tract and anus have been associated with HPV types 16, 18, 31, or 45, whereas most external genital warts are associated with HPV types 6 or 11 (6). Subclinical genital HPV infection occurs more frequently than visible genital warts and refers to manifestations of infection in the absence of visible genital warts, including situations where infection is diagnosed on the basis of characteristic cytologic features, squamous intraepithelial lesions (SIL), or on any genital skin by a viral nucleic acid (DNA or RNA) or capsid protein test for HPV. Recognition of the role of specific HPV types in cervical cancer and the advent of type-specific HPV tests have stimulated a focus on the use of HPV diagnostic tests in prevention of cervical cancer. Testing for HPV was recently proposed as a strategy to determine which women with low-grade cervical cytologic abnormalities require colposcopic evaluation. Several trials designed to clarify the role of HPV testing in the evaluation of low-grade cervical abnormalities indicate that HPV testing can be useful in the management of women with Papanicolaou tests that show atypical squamous cells of undetermined significance, but not in the management of low-grade SIL (43, 44). At this time, data are insufficient to recommend routine HPV testing for other clinical purposes. No therapy has been identified that effectively eradicates persistent subclinical HPV infection. In the presence of coexistent SIL, management should be based on histopathologic findings and includes cryotherapy, laser ablation, cone biopsy, or loop electrosurgical excision procedure.

A strong relation exists among persistent HPV infection, anal SIL, and anal cancer, showing the same spectrum of HPV types as those associated with cervical cancer (45). Prevalence of anal SIL and anal cancer is substantially increased among men who have sex with men and men with HIV infection (46). Clinicians should be aware of the importance of intra-anal manifestations of HPV infection in such men, given the association of HPV with anal dysplasia, and they should consider anoscopic examination in persons with symptoms referable to the anal canal. However, high-grade anal SIL has been shown in normal-appearing anal mucosal biopsy specimens from men with and without HIV infection (47). The appropriate clinical management for persons with high-grade anal SIL is uncertain, but ablation or surgical removal has been sug-

gested. Because of the increased incidence of anal cancer in HIV-infected men who have sex with men, screening for anal SIL by anal cytologic examination has been proposed (48). However, because the natural history of anal SIL has not been established and management strategies are not clearly defined, such a screening approach cannot currently be recommended in the STD treatment guidelines.

CONCLUSIONS

For more than 20 years, the CDC's publication of national guidelines for STD management has been a key component of federal initiatives to improve the health of the U.S. population by preventing and controlling STDs and their sequelae. These public health goals can be attained only if they are supported by knowledgeable clinicians and if clinicians are, in turn, supported by health care systems that make it possible for them to deliver optimal care for patients with STDs and to incorporate new guidelines into clinical practice. The 2002 guidelines should therefore be viewed as the starting point for a process that requires the ongoing efforts of residency program directors, providers of continuing medical education, clinic managers, and health plan administrators in public and private sectors. As recommendations for STD treatment continue to evolve in response to basic and clinical research advances, emerging antimicrobial resistance, and changing sexual and health care behaviors, clinical practice—at both the individual and the system level—must reflect these changes. New, more effective treatment regimens; highly sensitive screening tests for asymptomatic infection; improvements in counseling of patients and their sexual partners; and new vaccines for sexually transmitted pathogens will benefit individual patients and be crucial to the achievement of our broader public health goal of improving sexual and reproductive health in the United States.

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