

Prevention and Treatment of Sexually Transmitted Diseases: An Update

MICHELE VAN VRANKEN, MD, *Teen Age Medical Service, Children's Hospitals and Clinics of Minnesota, Minneapolis, Minnesota*

The Centers for Disease Control and Prevention recently published revised guidelines for the prevention and treatment of sexually transmitted diseases. One new treatment strategy is the use of azithromycin as a primary, rather than alternative, medication for pregnant women with *Chlamydia trachomatis* infection. Quinolone-resistant *Neisseria gonorrhoeae* infection continues to increase in the United States; therefore, quinolones are no longer recommended for treatment of this infection. Expedited partner therapy gives physicians another option when addressing the need to treat partners of persons diagnosed with *N. gonorrhoeae* or *C. trachomatis* infection. Tinidazole is now available in the United States and can be used to manage trichomoniasis, including trichomoniasis resistant to metronidazole. Shorter courses of antiviral medication can be used for episodic therapy of recurrent genital herpes. Because of increasing resistance, close follow-up is required if azithromycin is used as an alternative treatment in the management of primary or secondary syphilis. Unexpected increases in the rates of lymphogranuloma venereum have occurred in the Netherlands, and physicians should remain vigilant for symptoms of this disease in the United States. (*Am Fam Physician* 2007;76:1827-32, 1833-34. Copyright © 2007 American Academy of Family Physicians.)

► **Patient information:** A handout on sexually transmitted diseases, written by the author of this article, is provided on page 1833.

The Centers for Disease Control and Prevention (CDC) recently released updated guidelines for the prevention and treatment of sexually transmitted diseases (STDs).¹ These guidelines were developed through a systematic review of evidence that has become available since the 2002 guidelines were issued, as well as through expert consultation.

Health Education

Education and counseling are the main strategies in the prevention and control of STDs. Evaluation includes addressing key areas of sexual health referred to as the Five P's: Partners, Prevention of pregnancy, Protection from STDs, Practices, and Past history of STDs. Addressing this information with patients creates an opportunity for physicians to provide counseling and education while taking into account each patient's individual risk factors and goals. The use of motivational interviewing focuses on the specific behaviors of the patient and places a greater emphasis on moving toward individually defined, achievable, risk-reduction

goals. *Table 1*¹ lists symptoms and diagnoses of selected STDs.

A visit with a physician for the screening, diagnosis, or treatment of STDs also provides an opportunity for the physician to educate the patient about human immunodeficiency virus (HIV). Patients may not be aware that the presence of an STD may facilitate the transmission of HIV if they are exposed to the virus. Because some patients who are HIV positive are unaware of their diagnosis, the CDC now encourages HIV screening for patients in all health care settings. Although patients may choose not to be tested, written consent for testing is no longer recommended (unless mandated by the state).²

Chlamydia Trachomatis

Chlamydia trachomatis is the most common reportable infectious disease in the United States, with almost 1 million cases reported in 2004.³ Few recommendations have changed for the treatment of persons infected with *C. trachomatis*; however, azithromycin (Zithromax) is now recommended as a primary, rather than alternative,

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References	Comments
Azithromycin (Zithromax) is recommended as a first-line treatment for <i>Chlamydia trachomatis</i> infection during pregnancy.	A	4-6	Based on randomized controlled trials
Quinolones should not be used in the treatment of <i>Neisseria gonorrhoeae</i> infection.	C	9	Based on expert opinion
Provision of expedited partner treatment lessens the risk of reinfection for patients treated for <i>N. gonorrhoeae</i> or <i>C. trachomatis</i> infection.	B	10-12	Based on limited randomized controlled trial evidence
Tinidazole (Tindamax) is an appropriate treatment option for metronidazole (Flagyl)-resistant trichomoniasis.	B	14, 16-18	Based on limited studies

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1760 or <http://www.aafp.org/afpsort.xml>.

treatment in pregnant women (Table 2).¹ This change occurred because of recent evidence supporting azithromycin as safe and effective during pregnancy.⁴⁻⁶

Neisseria Gonorrhoeae

Since the publication of the 2002 STD treatment guidelines, the rate of quinolone-resistant *Neisseria gonorrhoeae* has continued to increase throughout the United States. As resistance increases, recommendations continue to change. Previous recommendations focused on the high levels of resistance in areas of Asia and the Pacific, California, Hawaii, and in some specific

populations in the United States (e.g., men who have sex with men). In 2004, 6.8 percent of isolates collected by the CDC's Gonococcal Isolate Surveillance Project were resistant to ciprofloxacin (Cipro); when samples from California and Hawaii were excluded, 3.6 percent of isolates were resistant.⁷

Quinolone-resistant *N. gonorrhoeae* is more common in men who have sex with men than in men who have sex exclusively with women (23.8 versus 2.9 percent, respectively)⁷; however, the rate of quinolone-resistant *N. gonorrhoeae* continues to increase among heterosexual persons. In heterosexual men, the prevalence rose

Table 1. Symptoms and Diagnoses of Sexually Transmitted Diseases

Disease	Symptoms	Laboratory diagnosis
Chlamydia	Asymptomatic, or dysuria, discharge (penile or vaginal), pain with sex, abdominal or testicular pain, breakthrough bleeding	Nucleic acid amplification test of urine, endocervical sample, or urethral sample
Gonorrhea	Asymptomatic, or dysuria, discharge (penile or vaginal), pain with sex, abdominal or testicular pain, breakthrough bleeding	Nucleic acid amplification test of urine, endocervical sample, or urethral sample; gonococcal culture for rectal or pharyngeal specimens
Trichomoniasis	Asymptomatic, or vaginal discharge with odor or itching	Saline wet mount; rapid antigen testing; <i>Trichomonas</i> culture
Genital herpes simplex virus	Asymptomatic, or recurrent, painful vesicular or ulcerative lesions in the genital area	Viral culture; type-specific serologic test
Syphilis	Asymptomatic, or painless ulcer (chancere), systemic rash including palms and soles, cardiovascular and neurologic involvement	Serologic tests (nontreponemal and treponemal); darkfield examination
Lymphogranuloma venereum	Inguinal adenopathy, self-limited papule or ulcer, proctocolitis	Procedures not readily available to differentiate lymphogranuloma venereum from nonlymphogranuloma venereum <i>Chlamydia trachomatis</i>

Information from reference 1.

Table 2. Treatment of *Chlamydia trachomatis* Infection

Regimen	Agent	Dosage
Nonpregnant women		
Recommended	Azithromycin (Zithromax)	1 g orally once
	Doxycycline (Vibramycin)	100 mg orally twice daily for seven days
Alternative	Erythromycin base	500 mg orally four times daily for seven days
	Erythromycin ethylsuccinate	800 mg orally four times daily for seven days
	Ofloxacin (Floxin)*	300 mg orally twice daily for seven days
	Levofloxacin (Levaquin)	500 mg orally daily for seven days
Pregnant women		
Recommended	Azithromycin	1 g orally once
	Amoxicillin	500 mg three times daily for seven days
Alternative	Erythromycin base	500 mg four times daily for seven days
		or
		250 mg four times daily for 14 days†
	Erythromycin ethylsuccinate	800 mg four times daily for seven days
or		
	400 mg four times daily for 14 days†	

*—Brand no longer available in the United States.

†—Lower-dose erythromycin regimens may be considered if there is gastrointestinal intolerance to higher dosages.

Information from reference 1.

from 0.9 percent in 2002 to 3.8 percent in 2005,⁸ and preliminary data from the first six months of 2006 indicate an increase to 6.7 percent.⁹ Current guidelines reflect these changes (Table 3¹) by no longer recommending quinolones as treatment for *N. gonorrhoeae* infection.⁹

Expedited Partner Treatment

It is standard practice to recommend that sex partners of patients diagnosed with an STD be treated to decrease the risk of reinfection and to decrease the incidence and prevalence of STDs among social networks. The primary goal is for the patient's sex partners to be seen by a physician for testing, treatment, and education. However, there may be clinical situations in which this cannot be accomplished (e.g., because of patient, partner, or resource limitations). In these circumstances, the CDC recommends that physicians consider using expedited partner treatment.

Expedited partner treatment is the practice of treating sex partners of persons diagnosed with an STD without medical evaluation or prevention counseling; this is usually done by providing the patient with appropriate treatment to give to his or her partner. Three randomized controlled trials sponsored by the CDC evaluated the behavioral

and clinical outcomes of expedited partner treatment compared with traditional treatment programs through patient or physician referral. In summary, the evidence supports expedited partner treatment as an option in patients with *N. gonorrhoeae* or *C. trachomatis* infection¹⁰⁻¹²; however, it is important for physicians to be aware of their state's legal provision for this practice.

Table 3. Treatment of Uncomplicated *Neisseria gonorrhoeae* Infection

Regimen	Agent	Dosage
Cervical, urethral, or rectal infection		
Recommended	Ceftriaxone (Rocephin)	125 mg IM once
	Cefixime (Suprax)	400 mg orally once
Alternative	Single-dose cephalosporin regimens*	
Pharyngeal infection		
Recommended	Ceftriaxone	125 mg IM once

NOTE: Quinolones should not be used to treat *Neisseria gonorrhoeae* infection. All therapies should also include the treatment of *Chlamydia trachomatis* infection if it has not been ruled out.

IM = intramuscularly.

*—See original guidelines for specific dosages.

Information from reference 1.

Table 4. Treatment of Trichomoniasis

Regimen	Agent	Dosage
Recommended	Metronidazole (Flagyl)*	2 g orally once
	Tinidazole (Tindamax)*†	2 g orally once
Alternative	Metronidazole*	500 mg orally twice daily for seven days

*—Patients should be advised to avoid consuming alcohol during treatment with metronidazole or tinidazole. Abstinence from alcohol should continue for 24 hours after completion of metronidazole or 72 hours after completion of tinidazole.

†—Tinidazole is U.S. Food and Drug Administration pregnancy category C; its safety during pregnancy has not been well evaluated.

Information from reference 1.

Table 5. Treatment of Genital Herpes Simplex Virus

Type	Agent	Dosage
First clinical episode	Acyclovir (Zovirax)	400 mg orally three times daily for seven to 10 days
		or
		200 mg orally five times daily for seven to 10 days
Episodic therapy for recurrent genital herpes	Famciclovir (Famvir)	250 mg orally three times daily for seven to 10 days
	Valacyclovir (Valtrex)	1 g orally twice daily for seven to 10 days
	Acyclovir	400 mg orally three times daily for five days
		or
		800 mg orally twice daily for five days
	Famciclovir	800 mg orally three times daily for two days
		or
		125 mg orally twice daily for five days
	Valacyclovir	1 g orally twice daily for one day
		or
500 mg orally twice daily for three days		
Suppressive therapy for recurrent genital herpes	Acyclovir	1 g orally once daily for five days
		or
	Famciclovir	400 mg orally twice daily
	Valacyclovir	250 mg orally twice daily
		500 mg orally once daily*
	or	1 g orally once daily

*— This dosage may be less effective than other valacyclovir or acyclovir dosing regimens in patients with frequent recurrences (more than 10 per year).

Information from reference 1.

Trichomoniasis

Since publication of the 2002 STD treatment guidelines, options for the diagnosis and treatment of trichomoniasis have continued to improve. Tinidazole (Tindamax), a nitroimidazole that is similar to metronidazole (Flagyl), has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of trichomoniasis. A review of randomized controlled trials suggests that tinidazole is equivalent or superior to metronidazole, with the recommended metronidazole regimen resulting in cure rates of 90 to 95 percent and the recommended tinidazole regimen resulting in cure rates of 86 to 100 percent (Table 4).^{1,13} Additionally, it is estimated that approximately 2.5 to 5 percent of *Trichomonas vaginalis* isolates now show some level of resistance to metronidazole.^{1,14} Tinidazole has a higher serum half-life and better penetration into the genitourinary tissues,^{15,16} which suggests that it is a potential treatment for metronidazole-resistant trichomoniasis.^{14,17,18}

Diagnostic options for trichomoniasis have also expanded. Although the most common diagnostic method for trichomoniasis involves microscopy of vaginal secretions, the sensitivity of this method is only 60 to 70 percent. Additional FDA-approved, point-of-care tests include the Osom Trichomonas Rapid Test, which uses immunochromatographic capillary flow dipstick technology, and the BD Affirm VPIII Microbial Identification Test, which is a nucleic acid probe test. Both have a sensitivity of more than 83 percent and specificity of more than 97 percent; however, false-positive results are a concern in areas of low disease prevalence.¹

Genital Herpes Simplex Virus

Most persons infected with genital herpes simplex virus (HSV) do not show clinical signs of disease. However, antiviral treatments for persons with clinical symptoms provide some symptomatic relief, as well as a lower viral burden and potential for transmission. Additional alternatives for episodic treatment of recurrent genital HSV require a shorter duration of treatment (one or two days of treatment versus five days of

treatment) (Table 5¹). Suppressive therapy can reduce genital HSV recurrences by 70 to 80 percent in patients with at least six recurrences per year¹; however, in the revised guidelines, there is greater emphasis on the use of suppressive therapy to reduce disease transmission. One study of daily treatment with 500 mg of valacyclovir (Valtrex) decreased the rate of viral transmission in heterosexual partners.¹⁹ Patients with HSV are encouraged to consider suppressive treatment as part of the overall strategy in reducing transmission, regardless of the number of recurrences per year.

Syphilis

Rates of primary and secondary syphilis increased for the fifth consecutive year in 2005 (8,176 cases reported) to their highest levels since 1997.¹ Penicillin G benzathine continues to be the primary antibiotic treatment recommended (Table 6¹). The CDC guidelines also include a discussion of treatment with doxycycline (Vibramycin), tetracycline, and ceftriaxone (Rocephin) in patients who are allergic to penicillin. The use of azithromycin is also discussed. Although earlier studies suggested that azithromycin given as a single 2-g dose might be effective,^{20,21} several cases of treatment failure, as well as reported cases of isolate resistance have been noted, suggesting that close follow-up is needed if azithromycin is used.²²

Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is caused by *C. trachomatis* serovars L1, L2, or L3. Although still relatively uncommon in the United States and in western European countries, a significant increase in cases was noted in the Netherlands in 2004 among men who have sex with men.²³ The CDC addresses this concern by adding information to the guidelines about the clinical presentation of LGV. Presentation can include a nontender papule that may ulcerate after three to 30 days at the site of inoculation, and signs of proctocolitis (e.g., mucoid or hemorrhagic discharge, anal pain, constipation, fever or tenesmus) in persons with a history of rectal exposure to the bacteria. These symptoms in

Table 6. Treatment of Syphilis

Type	Agent	Dosage
Primary, secondary, and early latent	Penicillin G benzathine	2.4 million units IM once
Late latent, latent of unknown duration, and tertiary	Penicillin G benzathine	2.4 million units IM weekly for three weeks

IM = intramuscularly.

Information from reference 1.

Table 7. Treatment of Lymphogranuloma Venereum

Regimen	Agent	Dosage
Recommended	Doxycycline (Vibramycin)	100 mg orally twice daily for 21 days
Alternative*	Erythromycin base	500 mg orally four times daily for 21 days

*—Some specialists believe that azithromycin (Zithromax) 1 g orally weekly for three weeks is an effective treatment option, but data are lacking.

Information from reference 1.

at-risk patients should prompt further diagnostic and treatment consideration. Diagnosis is primarily clinical because culture and nucleic acid amplification testing are not specific for LGV caused by *C. trachomatis*. If a patient has symptoms and specific typing is desired, contact with state or local health departments is often required. The CDC continues to recommend a three-week course of doxycycline when symptoms or testing suggest LGV, although erythromycin is an alternative (Table 7¹).

The Author

MICHELE VAN VRANKEN, MD, is a family physician at Teen Age Medical Service, Children's Hospital and Clinics of Minnesota in Minneapolis. She also is the medical director of the Annex Teen Clinic in Robbinsdale, Minn., and the West Suburban Teen Clinic in Excelsior, Minn. Dr. Van Vranken received her medical degree from Rush Medical College in Chicago, Ill., and completed a family medicine residency and community and adolescent fellowship at the Ramsey Family and Community Medicine Residency Program, Minneapolis. She also has a certificate of added qualification in adolescent medicine.

Address correspondence to Michele Van Vranken, MD, Teen Age Medical Service, Children's Hospitals and Clinics of Minnesota, 2425 Chicago Ave. S., Minneapolis, MN 55404 (e-mail: michele.vanvranken@childrensmn.org). Reprints are not available from the author.

Author disclosure: Nothing to disclose.

REFERENCES

1. Workowski KA, Berman SM; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006 [Published correction appears in MMWR Recomm Rep. 2006;55(36):997]. MMWR Recomm Rep. 2006;55(RR-11):1-94.
2. Branson BM, Handsfield HH, Lampe MA, et al.; Centers for Disease and Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep. 2006;55(RR-14):1-17.
3. Jajosky RA, Hall PA, Adams DA, et al.; Centers for Disease Control and Prevention. Summary of notifiable diseases—United States, 2004. MMWR Morb Mortal Wkly Rep. 2006;53(53):1-79.
4. Jacobson GF, Autry AM, Kirby RS, Liverman EM, Motley RU. A randomized controlled trial comparing amoxicillin and azithromycin for the treatment of *Chlamydia trachomatis* in pregnancy. Am J Obstet Gynecol. 2001;184(7):1352-1354.
5. Kacmar J, Cheh E, Montagno A, Peipert JF. A randomized trial of azithromycin versus amoxicillin for the treatment of *Chlamydia trachomatis* in pregnancy. Infect Dis Obstet Gynecol. 2001;9(4):197-202.
6. Rahangdale L, Guerry S, Bauer HM, et al. An observational cohort study of *Chlamydia trachomatis* treatment in pregnancy. Sex Transm Dis. 2006;33(2):106-110.
7. U.S. Dept. of Health and Human Services. Sexually transmitted disease surveillance 2004 supplement. Gonococcal Isolate Surveillance Project (GISP) annual report 2004. Atlanta, Ga.: Centers for Disease Control and Prevention, National Center for HIV, STD, and TB Prevention, Division of STD Prevention, 2005. <http://www.cdc.gov/std/GISP2004/GISP2004.pdf>. Accessed July 17, 2007.
8. U.S. Dept. of Health and Human Services. Sexually transmitted disease surveillance 2005 supplement. Gonococcal Isolate Surveillance Project (GISP) annual report 2005. Atlanta, Ga.: Centers for Disease Control and Prevention, National Center for HIV, STD, and TB Prevention, Division of STD Prevention, 2007. <http://www.cdc.gov/std/GISP2005/GISPSurvSupp2005short.pdf>. Accessed July 17, 2007.
9. Centers for Disease and Control and Prevention. Update to CDC's sexually transmitted diseases treatment guidelines, 2006: fluoroquinolones no longer recommended for treatment of gonococcal Infections. MMWR Morb Mortal Wkly Rep. 2007;56(14):332-336.
10. Schillinger JA, Kissinger P, Calvet H, et al. Patient-delivered partner treatment with azithromycin to prevent repeated *Chlamydia trachomatis* infection among women: a randomized, controlled trial. Sex Transm Dis. 2003;30(1):49-56.
11. Golden MR, Whittington WL, Handsfield HH, et al. Effect of expedited treatment of sex partners on recurrent or persistent gonorrhoeae or chlamydial infection. N Engl J Med. 2005;352(7):676-685.
12. Kissinger P, Mohammed H, Richardson-Alston G, et al. Patient-delivered partner treatment for male urethritis: a randomized, controlled trial. Clin Infect Dis. 2005;41(5):623-629.
13. Forna F, Gülmezoglu AM. Interventions for treating trichomoniasis in women. Cochrane Database Syst Rev. 2003;(2):CD000218.
14. Sobel JD, Nyirjesy P, Brown W. Tinidazole therapy for metronidazole-resistant vaginal trichomoniasis. Clin Infect Dis. 2001;33(8):1341-1346.
15. Schmid G, Narcisi E, Mosure D, Secor WE, Higgins J, Moreno H. Prevalence of metronidazole-resistant *Trichomonas vaginalis* in a gynecology clinic. J Reprod Med. 2001;46(5):545-549.
16. Sawyer PR, Brogden RN, Pinder RM, Speight TM, Avery GS. Tinidazole: a review of its antiprotozoal activity and therapeutic efficacy. Drugs. 1976;11(6):423-440.
17. Hager WD. Treatment of metronidazole-resistant *Trichomonas vaginalis* with tinidazole: case reports of three patients. Sex Transm Dis. 2004;31(6):343-345.
18. Hamed KA, Studemeister AE. Successful response of metronidazole-resistant trichomonal vaginitis to tinidazole. A case report. Sex Transm Dis. 1992;19(16):339-340.
19. Corey L, Wald A, Patel R, et al.; Valacyclovir HSV Transmission Study Group. Once-daily valacyclovir to reduce the risk of transmission of genital herpes. N Engl J Med. 2004;350(1):11-20.
20. Hook EW, Martin DH, Stephens J, Smith BS, Smith K. A randomized, comparative pilot study of azithromycin versus benzathine penicillin G for treatment of early syphilis. Sex Transm Dis. 2002;29(8):486-490.
21. Riedner G, Rusizoka M, Todd J, et al. Single-dose azithromycin versus penicillin G benzathine for the treatment of early syphilis. N Engl J Med. 2005;353(12):1236-1244.
22. Lukehart SA, Godornes C, Molini BJ, et al. Macrolide resistance in *Treponema pallidum* in the United States and Ireland. N Engl J Med. 2004;351(2):154-158.
23. Centers for Disease Control and Prevention. Lymphogranuloma venereum among men who have sex with men—Netherlands, 2003-2004. MMWR Morb Mortal Wkly Rep. 2004;53(42):985-988.