

# Management of Uncomplicated *Chlamydia trachomatis* Infections in Adolescents and Adults: Evidence Reviewed for the 2006 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines

**William M. Geisler**

Department of Medicine, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham

In April 2005, in preparation for the 2006 Centers for Disease Control and Prevention (CDC) sexually transmitted diseases (STD) treatment guidelines, the CDC convened an advisory group to examine recent abstracts and published literature addressing management of *Chlamydia trachomatis* infections in adolescents and adults. Key questions were posed and answered on the basis of quality of evidence and expert opinion. Clinical trials continue to demonstrate equivalent efficacy and tolerability of azithromycin and doxycycline regimens, and both remain recommended as first-line therapy in nonpregnant individuals. More data and clinical experience are available to support the efficacy, safety, and tolerability of azithromycin in pregnant women, and, in the upcoming guidelines, azithromycin will be recommended as first-line therapy for such patients. Evidence is building that expedited partner therapy (EPT), with provision of treatment or a prescription, may be just as effective as or more effective than standard partner referral in ensuring partner treatment and preventing chlamydia recurrence in women. Although there are more studies needed and barriers to be addressed before its widespread use, EPT will be recommended as an option for partner management.

Chlamydial genital infection is the most frequently reported bacterial sexually transmitted disease (STD) in the United States [1], and its prevalence is highest among persons  $\leq 25$  years of age [2]. Asymptomatic chlamydial infection is common among both men and women, and detection often relies on screening. The Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force each recommend annual chlamydial screening for all sexually active women  $\leq 25$  years of age and also for older women with risk factors (e.g., those who have a new sex partner or multiple sex partners) [3, 4]. The benefits of chla-

mydial screening in women have been demonstrated in areas where screening programs have reduced both the prevalence of chlamydia [5, 6] and rates of pelvic inflammatory disease [7, 8].

The approach to the management of uncomplicated genital chlamydial infection in adults includes (1) treatment of patients (to reduce complications and prevent transmission to sex partners), (2) treatment of sex partners (to prevent reinfection of the index patient and infection of other partners), (3) risk-reduction counseling, and (4) repeat chlamydial testing in women a few months after treatment (to identify recurrent/persistent infections). After publication of the 2002 CDC STD treatment guidelines [3], there remained both unanswered questions and topics requiring further study in the approach to management of uncomplicated genital chlamydial infection. In April 2005, in preparation for the 2006 CDC STD treatment guidelines, the CDC convened an advisory

---

Reprints or correspondence: Dr. William M. Geisler, University of Alabama at Birmingham STD Program, 703 19th St. S, 242 Zeigler Research Bldg., Birmingham, AL 35294-0007 (wgeisler@uab.edu).

**Clinical Infectious Diseases** 2007;44:S77-83

© 2007 by the Infectious Diseases Society of America. All rights reserved.

1058-4838/2007/4407S3-0002\$15.00

DOI: 10.1086/511421

group to examine recent abstracts and published literature addressing management of *Chlamydia trachomatis* infections in adolescents and adults.

The present article summarizes the key questions posed and evidence reviewed for the management of uncomplicated *C. trachomatis* infections that were considered in the development of the 2006 CDC STD treatment guidelines. Some key questions revisited topics such as (1) considerations for recommending doxycycline versus azithromycin; (2) the efficacy, tolerability, and safety of azithromycin in pregnant women; and (3) the interval for performing repeat chlamydial testing after treatment in women. Other key questions addressed topics not previously reviewed for the CDC STD treatment guidelines, including (1) the role of expedited partner therapy (EPT) for management of sex partners, (2) routine chlamydial screening in men, and (3) repeat chlamydial testing in men after treatment.

## SUBJECTS AND METHODS

A search of the literature from 2000 through 2004 was conducted with the Medline computerized database of the US National Library of Medicine. The terms “chlamydia infections” (as subject heading) and “drug therapy,” “therapy,” and “prevention and control” (as subheadings) were combined, exploded, limited to the years 2000–2004, and searched for in titles and abstracts. The combined search was limited to human subjects and to persons  $\geq 13$  years of age. This yielded a total of 397 citations. The search was further limited to not include articles exclusively discussing *Chlamydophila pneumoniae*; this reduced the number of citations to 351. Citations were then selected from this group if their content included chlamydia treatment (for patients or their sex partners) or repeat (recurrent/persistent) infections after treatment. Abstracts discussing chlamydia therapy from national scientific meetings from 2000 through 2004 were also reviewed. If an abstract was published or in press in manuscript form, then preference was given to data from the manuscript. Articles or abstracts were then summarized, including information on study design, methodology, results, and conclusions. In addition, we reviewed selected articles published during 1996–1999 that were previously reviewed for the 2002 CDC STD treatment guidelines.

The quality of the resulting literature and abstracts from the search was then rated as good, moderate, or insufficient. The quality of the evidence and discussions with expert consultants were then used to address key questions on the management of chlamydial infections in adolescents and adults and to formulate recommendations for the upcoming 2006 CDC STD treatment guidelines.

## RESULTS

### What Are the Considerations for Recommending Doxycycline versus Azithromycin Regimens for Uncomplicated Genital Chlamydial Infection, and Should Both Remain First-Line Treatment for Nonpregnant Individuals in the 2006 CDC STD Treatment Guidelines?

**Cost.** Although the average wholesale cost of azithromycin (1 g single dose) is higher than the cost of a 7-day course of doxycycline (100 mg twice daily), one must consider that some patients who receive the 7-day doxycycline regimen may take only a few doses, which could result in treatment failure and put them at risk for persistence of uncomplicated infection and/or development of upper genital tract complications. Hence, the higher cost of azithromycin must be balanced against the medical cost of potential complications of persistent infection that could result from treatment failure in noncompliant doxycycline-treated patients. Decision analysis studies have demonstrated that single-dose azithromycin is just as cost-effective as—or more cost-effective than—a 7-day course of doxycycline [9, 10].

**Efficacy.** Most efficacy studies of therapy for chlamydia have relied on measuring outcome (i.e., test of cure) with diagnostic tests that have sensitivity lower than that of nucleic acid amplification tests. Thus, an evolving concern is whether current therapy is simply suppressing the organism, as opposed to truly eradicating it. In a recent meta-analysis of 12 randomized clinical trials of azithromycin versus doxycycline for genital chlamydial infections, Lau and Qureshi [11] found that microbial cure rates (based on culture in 9 of the 12 trials) were 97% and 98%, respectively; after the data were pooled, the efficacy difference for microbial cure between the 2 drugs was not statistically significant.

**Compliance.** One concern about the currently recommended doxycycline regimen is compliance. Two recent studies have documented noncompliance with doxycycline. In an observational study of doxycycline compliance in STD clinics in Brooklyn, New York, and Birmingham, Alabama, reported by Augenbraun et al. [12], 24% of patients were noncompliant, and 51% had only “intermediate” compliance as measured by Medication Event Monitoring System technology (APREX). In a related study performed at an STD clinic in Birmingham, Alabama, Bachmann et al. [13] assessed Medication Event Monitoring System—measured versus self-reported doxycycline compliance. They found that, although 90% of patients reported taking their medication as directed, only 33% were fully compliant on the basis of measurement by the Medication Event Monitoring System; 65% took  $>11$  of the 14 doses, but 67% had at least 1 period of  $\geq 24$  h between doses. The extent to which noncompliance with the current doxycycline regimen affects its efficacy remains unclear. In the study by Bachmann

et al. [13], when therapeutic success was measured in the 81 participants with initially positive chlamydial culture results, follow-up PCR results were positive in only 6%, suggesting a “margin of error” in the 7-day regimen and indicating that the level of compliance achieved led to cure rates similar to those reported in earlier doxycycline efficacy studies.

**Adverse reactions.** Serious adverse events (including allergic reactions) are uncommon with both azithromycin and doxycycline. In the meta-analysis by Lau et al. [11], adverse events occurred in 25% and 23% of individuals treated with azithromycin and doxycycline, respectively; after the data were pooled, the risk difference for adverse events was not statistically significant.

**Summary.** Clinical trials continue to demonstrate equivalent efficacy and tolerability of azithromycin versus doxycycline regimens for chlamydial infections. Each antibiotic regimen has advantages or disadvantages in terms of cost, convenience, and compliance, yet both regimens will remain recommended as first-line therapy for uncomplicated chlamydial infection in nonpregnant individuals.

#### **Do Efficacy and Tolerability of Azithromycin Differ by Formulation (Sachet vs. Tablets)?**

No new data were available to answer this question. Anecdotal evidence suggests that people have varying abilities to tolerate different formulations (sachet vs. tablets), but the impact of different formulations on efficacy is unclear.

**Summary.** There are insufficient data on the efficacy and tolerability of different formulations of azithromycin to provide recommendations for the 2006 CDC STD treatment guidelines.

#### **Are Alternative Regimens of Doxycycline Effective (e.g., 100 mg Daily for 7 Days, 200 mg Daily for 7 Days, and Other Regimens)?**

There were no new studies that addressed this question since the 2002 CDC STD treatment guidelines were published.

**Summary.** There remain insufficient data on the efficacy of alternative regimens of doxycycline to recommend any regimens other than the currently recommended regimen of 100 mg twice daily for 7 days.

#### **What Are the Most Efficacious and Best-Tolerated Therapies for Pregnant Women, and Should Erythromycin and Amoxicillin Regimens Remain as First-Line Recommended Therapy?**

In the 2002 CDC STD treatment guidelines, recommended therapies for chlamydia in pregnant women were erythromycin base (500 mg 4 times daily for 7 days) or amoxicillin (500 mg 3 times daily for 7 days), with single-dose azithromycin (1 g) listed as an alternative regimen [3]. Two clinical trials, reviewed for the 2002 CDC STD treatment guidelines, comparing single-

dose azithromycin (1 g) versus erythromycin (500 mg 3 or 4 times daily for 7 days) in pregnant women with chlamydia revealed azithromycin to be highly efficacious [14, 15]. Azithromycin was also better tolerated than erythromycin, as reflected by the fact that early discontinuation of erythromycin was common [14, 15]. In the randomized, unblinded clinical trial by Adair et al. [14] comparing azithromycin and erythromycin among 106 pregnant women who had a positive chlamydia DNA probe result, azithromycin and erythromycin had similar efficacies (88% vs. 93%, respectively). Azithromycin was much better tolerated than erythromycin (gastrointestinal adverse effects occurred in 12% vs. 58% of patients, respectively) and, therefore, was less often discontinued because of adverse effects (2% vs. 19%, respectively; overall compliance, 98% vs. 54%, respectively) [14]. In the small study ( $n = 48$ ) by Wehbeh et al. [15], the efficacy of azithromycin (as assessed by culture) among 17 pregnant women and their partners was 95% at 4 weeks after treatment initiation, and the rate of discontinuation due to adverse effects was much lower among the pregnant women receiving azithromycin than among those receiving erythromycin (7% vs. 39%, respectively;  $P = .02$ ).

Two clinical trials comparing single-dose azithromycin (1 g) versus amoxicillin (500 mg 3 times daily for 7 days) in pregnant women with chlamydia were published after the release of the 2002 CDC STD treatment guidelines, and they revealed no significant differences in efficacy [16, 17]. However, both studies were insufficiently powered to detect significant differences and had other limitations. In the randomized controlled trial by Jacobson et al. [16], 129 pregnant women with chlamydia at 2 university-based clinics were randomized to receive azithromycin or amoxicillin regimens and then received a “test of cure” by chlamydial ligase chain reaction at 4 weeks after treatment initiation. Among the 110 patients (85%) who completed the study, the treatment efficacies of azithromycin and amoxicillin were similar (64% vs. 58%;  $P = .56$ ). One limitation of this study was that it included noncompliant patients within the group of patients with treatment failure in the analyses, which likely contributed to the unexpected low cure rates in this study. In the randomized, controlled, single-blind trial by Kacmar et al. [17], 39 pregnant women with chlamydia in a university hospital setting were randomized to receive azithromycin or amoxicillin regimens and then received a test of cure by chlamydial ligase chain reaction at 4–6 weeks after treatment completion. Among the 34 patients (87%) who completed the study, the test-of-cure results were positive in 1 (5%) of 19 women treated with azithromycin, versus 3 (20%) of 15 women who received amoxicillin ( $P = .3$ ). One limitation of this study was that 16% of women in the amoxicillin group did not take all of the treatment doses. Both studies assessed tolerability of azithromycin and amoxicillin regimens and

found no significant differences; however, they were insufficiently powered to detect significant differences. Jacobson et al. [16] reported that 10.9% of patients receiving azithromycin, versus 5.5% of those receiving amoxicillin regimens, were intolerant ( $P = .31$ ). Kacmar et al. [17] reported moderate to severe gastrointestinal intolerance in 40% in the azithromycin group, versus 17% in the amoxicillin group ( $P = .11$ ).

Theoretically, the use of amoxicillin for chlamydia in pregnant women could induce a persistent metabolically inactive form of chlamydia. Thus, a patient may have negative test-of-cure culture results yet may harbor viable organisms that become metabolically active at a later time, leading to clinical recurrence of infection. Such persistent chlamydial forms have been demonstrated in cell culture after exposure to penicillin. However, clinical studies to date have not been able to adequately address this concern, for  $\geq 1$  of the following reasons: (1) the study was insufficiently powered, (2) the study did not utilize sensitive nonculture tests (i.e., nucleic acid amplification tests), and (3) it was not possible to rule out patient reinfection from an untreated partner. It may be that, even if amoxicillin induces such persistent chlamydial forms in humans, the host immune response still eradicates the infection.

Finally, a retrospective cohort study by Rahangdale et al. [18] of 277 pregnant women with chlamydia evaluated by providers in a health maintenance organization reported that azithromycin (1) was the most commonly prescribed agent for chlamydia in pregnancy, followed by erythromycin and amoxicillin (69%, 19%, and 9%, respectively); and (2) had a treatment efficacy (i.e., negative test-of-cure at  $>7$  days after treatment) comparable to that of amoxicillin (97% vs. 95%) and significantly higher than that of erythromycin (64%). When the interval for the test of cure was limited to 3 weeks after treatment, the efficacies of azithromycin, amoxicillin, and erythromycin were 100%, 100%, and 50%, respectively ( $P < .0001$ ). Limitations of this study include the retrospective study design (i.e., the inherent limitations with chart review), the broad time interval within which tests of cure were performed (up to 224 days), and the lower sensitivity of the chlamydia diagnostic assays utilized (DNA hybridization probes).

**Summary.** Since the 2002 CDC STD treatment guidelines were published, more data and clinical experience have become available to support the efficacy and tolerability of single-dose azithromycin (1 g administered orally) for treatment of chlamydial infection in pregnant women. Accordingly, azithromycin will be recommended as a first-line agent for chlamydia treatment in pregnancy. Despite theoretical concerns that amoxicillin could induce a persistent chlamydial infection rather than microbiological cure, there are insufficient clinical data to support this concern; however, consideration should be given for using a non-culture-based test (i.e., nucleic acid amplification tests) for test of cure (at  $\geq 3$  weeks after treat-

ment) in pregnant women treated with amoxicillin. With current data demonstrating that the efficacy and tolerability of amoxicillin are similar to those of azithromycin, amoxicillin (500 mg 3 times daily for 7 days) will remain a first-line recommended antimicrobial regimen in pregnancy. Because of the high intolerance rate with erythromycin in pregnant women, which may increase noncompliance and decrease efficacy, erythromycin base (500 mg 4 times daily for 7 days) will be recommended as an alternative antimicrobial regimen for chlamydia therapy.

### **Is Azithromycin Safe in Pregnancy?**

Azithromycin is a pregnancy risk category B medication. Relatively few studies have been performed to address pregnancy or neonatal outcomes after azithromycin use for chlamydia treatment in pregnancy; however, the available data suggest that azithromycin is safe in pregnancy [14–18]. In the Rahangdale et al. [18] study, 280 infants were born to the 277 women in the study sample, and there were no significant differences in maternal or neonatal complications, preterm deliveries, 5-min Apgar scores, or congenital anomalies between azithromycin, amoxicillin, and erythromycin. In the Jacobson et al. [16] study, there were no significant differences in preterm delivery ( $<37$  weeks) between pregnant women with chlamydia receiving azithromycin and those receiving amoxicillin (13% vs. 16%).

**Summary.** Available data and clinical experience suggest that azithromycin is safe in pregnancy.

### **Is Azithromycin Safe and Effective in Adolescents, and at What Dose?**

No new published data were available to address this question. The advisory group and other experts who were consulted reported no safety problems with azithromycin use in adolescents, and they agreed that adolescents should receive a dose equivalent to that given to adults.

**Summary.** Although there are limited recent data on safety and efficacy of azithromycin in adolescents, there is vast clinical experience and a consensus in the advisory group that adolescents should receive azithromycin at a dose equivalent to that given to adults for chlamydia.

### **Does EPT (Delivered by the Patient or Provider) Reduce Chlamydial Reinfection, and Should It Be Recommended in the 2006 CDC STD Treatment Guidelines?**

EPT is the provision of medication or a prescription to a partner by the patient or provider. Three recent clinical trials addressed whether some form of EPT reduces chlamydial reinfection. Schillinger et al. [19] reported that, in a multicenter randomized controlled trial of patient-delivered partner therapy (PDPT) with azithromycin (1 g) versus standard partner referral in 1787 women with chlamydia, the rate of reinfection

(as assessed by ligase chain reaction or PCR) among 1454 women with  $\geq 1$  follow-up visit was lower, by 4 months after therapy, in the PDPT arm (12% vs. 15%, respectively), yet the difference only approached significance ( $P = .1$ ). Golden et al. [20] reported that, in a randomized controlled trial of EPT with azithromycin (1 g) (patient delivered or provider facilitated) versus partner referral (by patient or provider) in men or women with chlamydia, rates of recurrent or persistent infection (as assessed by ligase chain reaction or by the Gen-Probe Aptima Combo 2 [Gen-Probe]) among 1595 men and women with chlamydia were lower at 10–18 weeks after therapy with EPT (10.8% vs. 13.2%, respectively); again, however, the difference only approached significance ( $P = .17$ ). Interestingly, the Golden et al. [20] study also evaluated EPT with single-dose cefixime for gonorrhea versus standard partner referral and found that EPT was significantly more effective in reducing recurrent or persistent gonorrhea than was standard partner referral ( $P = .01$ ), perhaps suggesting differences in the efficacy of chlamydia versus gonorrhea treatment regimens in eradicating infection (outcome differences occurred primarily in women). A study by Kissinger et al. [21] evaluated the efficacy of PDPT with single-dose regimens of azithromycin plus ciprofloxacin or cefixime versus standard partner referral or booklet-enhanced partner referral for reducing recurrence of chlamydia and gonorrhea among 977 men with urethritis (76% of 931 men tested had chlamydia and/or gonorrhea). Of 79% of men who were re-interviewed 4–8 weeks after therapy, only 38% agreed to follow-up testing for chlamydia or gonorrhea. The PDPT and book-enhanced referral arms were significantly less likely than the standard referral arm to have a repeat positive test result for chlamydia or gonorrhea (23% and 14% vs. 43%, respectively;  $P < .001$ ). A limitation of this study was the combined, rather than individual, reporting of chlamydia and gonorrhea outcomes, which did not allow for the assessment of efficacy of the PDPT arm for preventing chlamydia recurrence.

In all of the EPT studies discussed above, patients utilizing EPT more often reported their partners receiving treatment. However, the proportion lost to follow-up in all of the studies was considerable and was a major limitation that could have influenced the study findings and conclusions. It is possible that, in some study patients (especially women), persistent infection (i.e., treatment failure) rather than reinfection may have occurred; this is suggested in the Golden et al. [20] study, in which the rate of repeat chlamydial detection among women who denied having had sexual intercourse after therapy was 8%, whereas it was 0% among male patients who denied having had intercourse after therapy. Even though these studies do not convincingly demonstrate the efficacy of partner-delivered therapy, they suggest that there is a trend toward decreasing chlamydia reinfection and that this intervention is at least as effective as standard

partner referral. EPT may still be cost-effective in averting complications of chlamydial infections. In a decision analysis model of cost-effectiveness (complications averted) by Postma et al. [22] that incorporated partner therapy (provision of prescriptions to partners) in chlamydial infections, partner therapy was found to reduce net costs per outcome averted by ~50%, compared with no partner therapy (i.e., partner referral).

Several questions and concerns regarding EPT need to be addressed before EPT is recommended for widespread routine practice. First, what are the legal constraints of this practice? The California State Senate adopted a bill paving the way for EPT in that state; in many other states, however, the legality of such practice is less clear. Second, EPT may reduce opportunities to screen partners for other STDs and to provide risk reduction education. Third, what are the medical risks, such as adverse drug reactions occurring in the partner (likely to be uncommon with azithromycin or doxycycline) or potential undertreatment of complicated chlamydial infection (e.g., pelvic inflammatory disease in a female partner)?

**Summary.** EPT has considerable potential public health benefit, is at least as effective as the current practice of standard partner referral, and will be recommended as an option for partner management of heterosexual male or female patients with chlamydia in the upcoming guidelines. Female partners should still be instructed to seek medical evaluation to assess for complications, such as pelvic inflammatory disease or other STDs, especially trichomoniasis [23]. Further studies are needed that address the efficacy and cost-effectiveness of EPT and the potential legal and medical risks (especially to female partners who have therapy delivered by male patients). At this time, EPT is not recommended as an option for chlamydia-infected men who have sex with men, because of insufficient clinical data on EPT in this population and because of concerns regarding the high prevalence of STDs (especially HIV infection) among their partners and the need to have these partners seen by a provider for STD testing.

#### **When Should Repeat Chlamydia Testing Be Performed in Women with Chlamydia after Therapy?**

Several recent studies have assessed repeat infection rates after chlamydial therapy [24–27]. However, the following differences in the studies made it difficult to define an optimal time for retesting women after therapy: (1) study design (retrospective versus prospective), (2) study population (e.g., general practice, STD clinic, reproductive health/family planning clinic, adolescent medicine clinic, school-based clinic, or correctional facility), (3) follow-up period (ranging from 2 weeks to 33 months), and (4) sensitivity of the diagnostic test utilized (e.g., nucleic acid amplification tests versus lower-sensitivity tests, including DNA probe or culture). On the basis of these studies and expert opinion, the advisory group felt that most repeat infections in

women would be detected if repeat testing was performed at ~3 months after therapy.

**Summary.** Repeat testing is necessary for women with chlamydia after therapy, because repeat infection is common; however, considerable differences in methodology among studies addressing repeat testing do not allow for the appropriate testing interval to be accurately determined. The advisory group came to the consensus that repeat testing at ~3 months was appropriate.

### **Should Routine Chlamydia Testing (i.e., Screening) Be Recommended for Men and, If So, in Which Clinical Settings?**

No new published data on routine screening in men could fully address this question. Young men may be more likely to seek a provider for STD evaluation if they have urethral symptoms rather than for routine screening. Because the majority of chlamydial infections in men are asymptomatic, routine chlamydial screening in men may be less feasible than it is in women, the latter of whom are more likely to be seen annually by providers, where chlamydial screening can be performed. The advisory group agreed that, although routine screening for *C. trachomatis* in sexually active young men may lead to a decrease in further transmission and, possibly, in sequelae in women, such screening should be considered to be optional until further studies are available to determine whether regular screening of all sexually active young men is feasible, efficacious, and cost-effective. Routine screening in men should, however, be considered in high-prevalence settings (e.g., adolescents, correctional facilities, and STD clinics).

**Summary.** Chlamydial testing in all sexually active men should not be considered to be a routine practice at this time, but it is a reasonable option if a patient is determined to be at risk for chlamydia or if resources permit such routine testing. Chlamydial testing should be considered for high-risk men (e.g., those with new or multiple sex partners and men who have sex with men) or in clinical settings with a high prevalence of chlamydia (e.g., adolescents, correctional facilities, and STD clinics).

### **Should Repeat Chlamydia Testing Be Recommended for Men with Chlamydia after Therapy, and, If So, in What Time Interval?**

No new published data were available to address this question. The frequency of repeat chlamydial infection in men after treatment is unknown, but it is probably high. It would be important for future studies to demonstrate that repeat testing in men decreased the prevalence of chlamydia among men and women, as well as complications in women. Some experts in the advisory group suggested that repeat testing at ~3 months after therapy be considered in men (same as for women)

**Summary.** Some experts recommend repeat testing in men

with chlamydia at ~3 months after therapy, although there are insufficient data to support this as a routine recommendation at this time.

### **Acknowledgments**

I am grateful to Byron Batteiger for his thoughtful review of this article.

**Financial support.** Sexually Transmitted Disease Faculty Expansion Program (grant R30 CCR421113), Centers for Disease Control and Prevention.

**Supplement sponsorship.** This article was published as part of a supplement entitled "Sexually Transmitted Diseases Treatment Guidelines," sponsored by the Centers for Disease Control and Prevention.

**Potential conflicts of interest.** W.M.G. is on the Pfizer speakers' bureau.

### **References**

1. Cates W. Estimates of the incidence and prevalence of sexually transmitted diseases in the United States. *Sex Transm Dis* **1999**; *26*:S2–7.
2. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2002 supplement. Chlamydia Prevalence Monitoring Project annual report 2002. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, October **2003**.
3. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *MMWR Recomm Rep* **2002**; *51*(RR-6):1–78.
4. US Preventive Services Task Force. Screening for chlamydial infection: recommendations and rationale. *Am J Prev Med* **2001**; *20*(Suppl 3): 90–4.
5. Mertz KJ, Levine WC, Mosure DJ, Berman SM, Dorian KJ, Hadgu A. Trends in the prevalence of chlamydial infections: the impact of community-wide testing. *Sex Transm Dis* **1997**; *24*:169–75.
6. Centers for Disease Control and Prevention. *Chlamydia trachomatis* genital infections United States, 1995. *MMWR Morb Mortal Wkly Rep* **1997**; *46*:193–8.
7. Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK, Stamm WE. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med* **1996**; *334*:1362–6.
8. Kamwendo F, Forslin L, Bodin L, Danielsson D. Decreasing incidences of gonorrhoea- and chlamydia-associated acute pelvic inflammatory disease: a 25-year study from an urban area of central Sweden. *Sex Transm Dis* **1996**; *23*:384–91.
9. Petitta A, Hart SM, Bailey EM. Economic evaluation of three methods of treating urogenital chlamydial infections in the emergency department. *Pharmacotherapy* **1999**; *19*:648–54.
10. Magid D, Douglas JM Jr, Schwartz JS. Doxycycline compared with azithromycin for treating women with genital *Chlamydia trachomatis* infections: an incremental cost-effectiveness analysis. *Ann Intern Med* **1996**; *124*:389–99.
11. Lau CY, Qureshi AK. Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials. *Sex Transm Dis* **2002**; *29*:497–502.
12. Augenbraun M, Bachmann L, Wallace T, et al. Compliance with doxycycline therapy in sexually transmitted diseases clinics. *Sex Transm Dis* **1998**; *25*:1–4.
13. Bachmann LH, Stephens J, Richey CM, Hook EW 3rd. Measured versus self-reported compliance with doxycycline therapy for chlamydia-associated syndromes: high therapeutic success rates despite poor compliance. *Sex Transm Dis* **1999**; *26*:272–8.
14. Adair CD, Gunter M, Stovall TG, et al. Chlamydia in pregnancy: a randomized trial of azithromycin and erythromycin. *Obstet Gynecol* **1998**; *91*:165–8.
15. Wehbeh HA, Ruggierio RM, Shahem S, et al. Single-dose azithromycin for *Chlamydia* in pregnant women. *J Reprod Med* **1998**; *43*:509–14.
16. Jacobson GF, Autry AM, Kirby RS, et al. A randomized controlled trial

- comparing amoxicillin and azithromycin for the treatment of *Chlamydia trachomatis* in pregnancy. *Am J Obstet Gynecol* **2001**;184:1352–4.
17. 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**;9:197–202.
  18. Rahangdale L, Guerry S, Bauer HM, et al. An observational cohort study of *Chlamydia trachomatis* treatment in pregnancy. *Sex Transm Dis* **2006**;33:106–10.
  19. 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**;30:49–56.
  20. Golden MR, Whittington WLH, Handsfield HH, et al. Impact of expedited sex partner treatment on recurrent or persistent gonorrhea or chlamydial infection. *N Engl J Med* **2005**;352:676–85.
  21. Kissinger P, Mohammed H, Richardson-Alston G, et al. Patient-delivered partner treatment for male urethritis: a randomized controlled trial. *Clin Infect Dis* **2005**;41:623–9.
  22. Postma MJ, Welte R, van den Hoek JA, et al. Cost-effectiveness of partner pharmacotherapy in screening women for asymptomatic infection with *Chlamydia trachomatis*. *Value Health* **2001**;4:266–75.
  23. Khan A, Fortenberry JD, Juliar BE, et al. The prevalence of chlamydia, gonorrhea, and trichomonas in sexual partnerships: implications for partner notification and treatment. *Sex Transm Dis* **2005**;32:260–4.
  24. Xu F, Schillinger JA, Markowitz LE, et al. Repeat *Chlamydia trachomatis* infection in women: analysis through a surveillance case registry in Washington State, 1993–1998. *Am J Epidemiol* **2000**;152:1164–70.
  25. Kjaer HO, Dimcevski G, Hoff G, et al. Recurrence of urogenital *Chlamydia trachomatis* infection evaluated by mailed samples obtained at home: 24 weeks' prospective follow up study. *Sex Transm Infect* **2000**;76:169–72.
  26. Whittington WL, Kent C, Kissinger P, et al. Determinants of persistent and recurrent *Chlamydia trachomatis* infection in young women: results of a multicenter cohort study. *Sex Transm Dis* **2001**;28:117–23.
  27. Burstein GR, Snyder MH, Conley D, et al. Adolescent chlamydia testing practices and diagnosed infections in a large managed care organization. *Sex Transm Dis* **2001**;28:477–83.