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Neglected Parasitic Infections in the United States: Trichomoniasis

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Abstract. *Trichomonas vaginalis* is one of the most common human parasitic infections in the United States, as well as the most prevalent non-viral sexually transmitted infection. However, it has long received much less consideration than other parasitic and sexually transmitted diseases. Much of this inattention can be attributed to a poor understanding of the public health impact of trichomoniasis. Increasing recognition of the sequelae of infection, including increased risk of infection with human immunodeficiency virus and adverse outcomes of pregnancy, has led to increased interest in *T. vaginalis*. Recent innovations include development of diagnostic tests that could improve detection of the parasite. A number of important questions, such as the epidemiology among men and women, the true public health burden of symptomatic and asymptomatic *T. vaginalis* infections, and whether current treatments will be adequate to reduce the substantial health disparities and costs associated with trichomoniasis, need consideration to remedy neglect of this important disease.

INTRODUCTION

Trichomoniasis is a sexually transmitted disease (STD) caused by the protozoan parasite *Trichomonas vaginalis*. With an estimated worldwide incidence of 248 million new cases per year, *T. vaginalis* infection is more common than *Chlamydia*, gonorrhea, and syphilis infections combined, making it the most common non-viral sexually transmitted infection (STI).[1] Despite this incidence, research and control efforts for *T. vaginalis* infection have traditionally lagged far behind efforts to control other STIs. It also disproportionately affects minorities and low-income populations, further contributing to its classification as a neglected parasitic infection.[2,3]

Although it affects both sexes, the health impact of trichomoniasis is manifested primarily in women. Clinically, *T. vaginalis* infections in women are usually asymptomatic, or symptoms can appear weeks, months or years after an initial infection.[4,5] Symptomatic trichomoniasis can cause mild to moderate inflammation of the cervix, vagina, and urethra.[6,7] Vaginal discharge can be copious, malodorous, and frothy. Pruritus and pain with urination or sexual intercourse may also be presenting complaints. Punctate hemorrhagic lesions in the genital epithelium can result in colpitis macularis or strawberry cervix, which is a specific sign for trichomoniasis.[6,7] Without appropriate treatment, *T. vaginalis* infection may persist for months to years.[8] In addition to these manifestations, trichomoniasis during pregnancy has been associated with premature rupture of the amniotic sac and chorion, preterm labor, and delivery of a low birth weight infant.[9–11] Women infected with human immunodeficiency virus (HIV) who are also infected with *T. vaginalis* have a higher risk of developing pelvic inflammatory disease.[12] *Trichomonas vaginalis* infections have also been linked to increased risks of other STDs:[13–21] infection is associated with 1.5–2.7 times greater risks of HIV acquisition and transmission[13–17] and up to a four-fold increase in HIV shedding.[18]

Trichomoniasis in men is not nearly as well studied or understood as it is in women. There are no licensed diagnostic assays for *T. vaginalis* infection in men, the occurrence of symptomatic infections is rare compared with the estimated prevalence of infection in males, and most infections are believed to resolve in the absence of treatment.[22] However, this perspective may be incomplete.[23] In addition, because infected men are often asymptomatic, they may be unaware of the risks to themselves and their sexual partners. For symptomatic men, the most common syndrome is urethritis. HIV-infected men with urethritis who are also infected with *T. vaginalis* have higher concentrations of HIV in their semen than HIV-infected men with urethritis who are not infected with *T. vaginalis*.[24] A potential link between *T. vaginalis* infection and prostate cancer has been hypothesized but remains controversial.[25,26]

Infection is most commonly diagnosed by identifying the motile parasite during microscopic examination of genital secretions (wet mount), usually cervico-vaginal secretions from women. However, the sensitivity of wet mount is generally poor (51–65%), and decreases by as much as 20% within one hour after collection.[27–29] Culture has been considered the gold standard method of diagnosis, but is time-consuming and costly, and therefore is not often performed in the clinical setting. Furthermore, diagnosis by culture requires a return visit for treatment, which can be a barrier to delivery of appropriate therapy. The first nucleic acid amplification test (NAAT) for *T. vaginalis* infection in women was cleared by the U.S. Food and Drug Administration in 2011.[30] The NAAT has high sensitivity and specificity and can be used to test genital secretions or urine specimens. Rapid point-of-care tests that detect parasite antigens or multi-copy genetic biomarkers have also been developed.[31–33] Sensitive tests that can provide accurate results within 30 minutes are advantageous because therapy can be prescribed or provided at the initial visit, which decreases missed treatment opportunities because of loss to follow-up.

The Centers for Disease Control and Prevention (CDC) guidelines recommend that all women seeking care for vaginal discharge should be tested for trichomoniasis.[34] Screening for *T. vaginalis* infection is recommended for all HIV-infected women upon entry to care and at least annually thereafter. In addition, screening can be considered for asymptomatic women at high risk for infection or disease (e.g., with a history

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of any STD, new or multiple sex partners, receiving care in a high-prevalence setting, or other risk factors).[34] Few data are available to guide testing or screening recommendations for men.

Nitroimidazoles (i.e., metronidazole or tinidazole) are the only class of antimicrobial medication approved for the treatment of trichomoniasis in the United States. In particular, metronidazole is an inexpensive, widely available, effective and generally well-tolerated treatment option. Treatment of all sex partners is recommended to reduce reinfection.[34]

However, nitroimidazoles may not be sufficient to treat all persons with trichomoniasis. Infections with antimicrobial-resistant *T. vaginalis* were identified in women with clinical treatment failure within a few years after metronidazole was introduced in the United States, although these findings might have been the result of naturally occurring nitroimidazole-tolerant strains rather than resistance that developed because of drug pressure. A recent study of STD clinic patients in six U.S. cities found that 4.3% of *T. vaginalis* isolates demonstrated low-level *in vitro* resistance to nitroimidazoles.[35] Host factors can also influence treatment efficacy. For example, HIV-infected women are less likely to respond to single-dose metronidazole treatment than HIV-uninfected women, even if the parasite isolate is drug sensitive *in vitro*. A longer nitroimidazole regimen may be needed for effective treatment of HIV-infected women who are also infected with *T. vaginalis*.[36]

In addition, occasional persons may report hypersensitivity reactions to nitroimidazole antimicrobial medications; this sensitivity is believed to be uncommon but the prevalence of this type of allergy is unknown. Most of these persons can be treated successfully for trichomoniasis without severe side effects by using an incremental dosing protocol.[37] However, persons who experience true anaphylactic reactions or Stevens-Johnson syndrome should not be retreated with nitroimidazoles.[38,39] No other Food and Drug Adminstration–approved treatments for trichomoniasis are available.

PUBLIC HEALTH IMPORTANCE OF TRICHOMONIASIS IN THE UNITED STATES

Trichomonas vaginalis is the most prevalent non-viral sexually transmitted infection and arguably the most common parasitic infection in the United States, affecting an estimated 3.7 million persons, including 2.3 million women and 1.4 million men nationwide.[4] A nationally representative study that used a sensitive polymerase chain reaction to detect *T. vaginalis* infections estimated a prevalence of 3.1% in U.S. women of reproductive age (14–49 years). Disparities are a prominent feature of this infection; non-Hispanic black women had the highest rates of infection at 13.3%, which is approximately 10 times higher than rates among Mexican-American (1.8%) or non-Hispanic white (1.3%) women.[2] Other risk factors identified in this study included lower socioeconomic status, lower educational levels, douching, and higher numbers of lifetime sex partners. Another nationally representative study of male and female adolescents tested for *T. vaginalis* infection by polymerase chain reaction reported that women were more likely than men to be infected (prevalence ratio = 1.64, 95% confidence interval = 1.25–2.15).[40]

In contrast to other non-viral STIs, *T. vaginalis* infection rates increase with age. In a metropolitan area with high STI rates, prevalence peaked among 51–60-year-old women, followed by women > 60 years of age and women 41–50 years of age.[41] A similar study conducted in men also showed a peak prevalence of *T. vaginalis* infection among 51–60 year-old men.[42] Thus, national estimates based on studies of persons < 50 years of age probably underestimate the true number of *T. vaginalis* infections in the United States.

Trichomoniasis is not a reportable condition in the United States or in any state.[43] As a result, the true incidence of infection has not been well established. Currently, CDC estimates that at least 1.1 million persons (including 680,000 women and 415,000 men) become infected with *T. vaginalis* each year.[4] Accurate measurements are complicated by the poor sensitivity of commonly used clinical testing methods (e.g., wet mount) and the large number of asymptomatic infections.

The cost and healthcare burden associated with trichomoniasis are substantial, and the direct medical costs are conservatively estimated to be $24 million per year in the United States.[44] The average lifetime cost per case has been estimated at $22, not including any costs associated with complications or associated conditions. However, persons infected with *T. vaginalis* may incur additional unrecognized costs because of adverse outcomes of pregnancy, HIV acquisition, or other health complications. For example, *T. vaginalis* infection may increase the risk of acquiring HIV; an estimated 2–6% of new HIV infections among U.S. women are attributable to trichomoniasis each year.[45,46] The estimated lifetime cost of these annual *T. vaginalis*-attributable HIV infections approaches $167 million.[46]

GAPS IN CURRENT KNOWLEDGE AND FUTURE DIRECTIONS

Despite its high prevalence and associated healthcare costs, many aspects of the pathology and public health impact of trichomoniasis remain poorly understood. The most pressing area of research is the epidemiology of the infection and the disease, including the incidence of symptomatic and asymptomatic infections, their respective risk factors, and sequelae that result if the patient is not treated. These data would help to determine whether there is a public health benefit to screening for *T. vaginalis* infections in persons with risk factors but without recognized symptoms. The recent availability of NAATs and point-of-cares tests may provide a more sensitive tool for identifying infection, but the optimal use of these tests will be difficult to define until there is a better understanding of the public health significance of asymptomatic infections. Clinical guidance is also needed with respect to using sensitive diagnostic tests after treatment to confirm microbiologic as well as clinical cure. One recent innovation has been using the Internet to offer free evaluations of self-collected specimens, a strategy that may reduce barriers to getting tested for STDs, as well as providing an additional source of epidemiologic data.[47,48] More investigation is also needed into host-parasite interactions that influence whether an infection is symptomatic. For example, parasite surface receptors that promote adherence to host epithelial cells may be key factors in pathogenesis.[49] Studies that investigate the long-term correlates and consequences of

symptomatic and asymptomatic infections will enable clinicians and public health practitioners to refine screening and treatment strategies.

A better understanding of the effects of trichomoniasis during pregnancy is also needed, including the best management of pregnant women with *T. vaginalis* infections and the potential long-term consequences for children born to infected mothers.[50] Despite the associations between infection and preterm delivery, limited data suggest that metronidazole treatment of pregnant women with asymptomatic infections does not reduce the risk of preterm delivery.[51] However, more well-designed studies using current diagnostic assays are needed to fully evaluate the risks and benefits of treating trichomoniasis during pregnancy.

Another unresolved question is whether some *T. vaginalis* infections may persist after treatment despite resolution of symptoms. Data that support this phenomenon include the association of increasing prevalence with age and the observation that a previous infection is a strong predictor of subsequent infection.[52] The association between *T. vaginalis* infection prevalence and age argue for public health strategies targeted to age groups not typically considered at high risk for STDs. In addition, longitudinal studies have identified some women who were negative for *T. vaginalis* after treatment, but subsequently were positive for parasites despite reporting no additional sexual activity.[53,54]

Persistent *T. vaginalis* infections despite clinical cure suggests that the problem of treatment failure may be more widespread than has been recognized. Although antimicrobial drug–resistant *T. vaginalis* clearly exists, not all treatment failures are solely attributable to parasite genetic characteristics; for example, many isolates received by the susceptibility testing service at CDC do not display resistance *in vitro*.[55] In addition, some women for whom nitroimidazole treatment failed during pregnancy can be cured with the same medication regimen after they have delivered. The exact mechanism of parasite resistance to nitroimidazoles and the host factors that contribute to overt or subclinical treatment failures remain major knowledge gaps that hinder comprehensive management of trichomoniasis.

Finally, the epidemiology of trichomoniasis in men should be evaluated more fully. For example, the putative association with prostate cancer should be confirmed or refuted with well-designed studies using sensitive diagnostic testing. There is also the question of whether more attention to *T. vaginalis* infections in men might reap public health benefits for women. Typically, men are offered treatment of trichomoniasis only if they have a female sex partner with a diagnosed infection. Although most of these men are infected,[5,56] their willingness to take antimicrobial medication may be decreased if they are not experiencing symptoms themselves. Many treatment failures in women are likely caused by reinfection after sex with an untreated or undertreated sex partner. Treatment of trichomoniasis in HIV-infected men has been shown to reduce HIV concentration in seminal fluid, leading to the suggestion that programs to control trichomoniasis in men could be a cost-effective approach to reducing HIV transmission.[24,57] Further study could also clarify the risk of trichomoniasis among men who have sex with men.

Publication of the *T. vaginalis* genome in 2007 provided a great step forward towards defining the genes responsible for parasite pathology and antimicrobial resistance.[58] However, fully understanding the genetic correlates of disease has been challenging because of the size, complexity, and repetitiveness of the genome. Nevertheless, population genetic analysis suggests that the preponderance of resistant isolates aggregate into one of two phylotypes.[59] This finding could lead to identification of genetic markers for resistance and the ability to develop molecular tests for isolates from persons who experience treatment failure, which could expedite results on drug susceptibility and improve patient care. Further research on the association of genetic markers with parasite virulence and persistence is also needed, including the effects of parasite infection with the *T. vaginalis* virus.[60,61]

One of the most important needs for improving case management will be identification of novel therapeutic regimens in instances when nitroimidazoles cannot be administered (e.g., antimicrobial resistance or hypersensitivity). If 4.3% of existing *T. vaginalis* infections demonstrate resistance to metronidazole, then more than 159,000 persons in the United States may require some form of alternative therapy. This figure is even higher when also considering the number of persons with severe hypersensitivity to nitroimidazoles. Because metronidazole treatment is inexpensive and effective for most trichomoniasis patients, financial incentives for pharmaceutical companies to develop new therapies are not large. However, we have recently identified some previously approved compounds that increase the efficacy of nitroimidazoles against resistant parasites *in vitro*[62]; combinations of these compounds with metronidazole or tinidazole also need *in vivo* evaluation. Intravaginal treatment with furazolidone or paromomycin sulfate treatment of women with severe hypersensitivity to the nitroimidazoles have been used with limited success,[63] but further study is needed. Similarly, intravaginal treatment with boric acid or betadine preparations has been effective for some women although additional evaluation will be necessary to confirm their efficacy.[64–66]

Trichomoniasis has long been overlooked as simply a nuisance infection, and persons who were not cured after treatment may have been judged noncompliant with therapy. Fortunately, these attitudes are changing and more emphasis is being placed on understanding the pathogenesis, burden, natural history, and response to treatment of *T. vaginalis* infection. Many important questions remain, including the current epidemiology of trichomoniasis among both men and women, the true public health burden of symptomatic and asymptomatic *T. vaginalis* infections, and whether current treatments will be adequate to reduce the substantial health disparities and costs associated with trichomoniasis. Increased emphasis on detection and treatment of infections is needed to move trichomoniasis out of the neglected category and to provide better care for those most impacted by this parasitic disease.

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REFERENCES

1. World Health Organization, 2011. *Prevalence and Incidence of Selected Sexually Transmitted Infections, Chlamydia trachomatis, Neisseria gonorrhoeae, syphilis and Trichomonas vaginalis: Methods and Results Used by WHO to Generate 2005 Estimates*. Available at: http://whqlibdoc.who.int/publications/2011/9789241502450_eng.pdf. Accessed February 8, 2013.
2. Sutton M, Sternberg M, Koumans EH, McQuillan G, Berman S, Markowitz L, 2007. The prevalence of *Trichomonas vaginalis* infection among reproductive-age women in the United States, 2001–2004. *Clin Infect Dis 45:* 1319–1326.
3. Van der Pol B, 2007. *Trichomonas vaginalis* infection: the most prevalent nonviral sexually transmitted infection receives the least public health attention. *Clin Infect Dis 44:* 23–25.
4. Satterwhite CL, Torrone E, Meites E, Dunne E, Mahajan R, Ocfemia MC, Su J, Xu F, Weinstock H, 2013. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. *Sex Transm Dis 40:* 187–193.
5. Seña AC, Miller WC, Hobbs MM, Schwebke JR, Leone PA, Swygard H, Atashili J, Cohen M, 2007. *Trichomonas vaginalis* infection in male sexual partners: implications for diagnosis, treatment, and prevention. *Clin Infect Dis 44:* 13–22.
6. Wølner-Hanssen P, Krieger JN, Stevens CE, Kiviat NB, Koutsky L, Critchlow C, DeRouen T, Hillier S, Holmes KK, 1989. Clinical manifestations of vaginal trichomoniasis. *JAMA 261:* 571–576.
7. Swygard H, Sēna AC, Hobbs MM, Cohen MS, 2003. Trichomoniasis: clinical manifestations, diagnosis and management. *Sex Transm Infect 80:* 91–95.
8. Peterman TA, Tian LH, Metcalf CA, Satterwhite CL, Malotte CK, DeAugustine N, Paul SM, Cross H, Rietmeijer CA, Douglas JM Jr, RESPECT-2 Study Group, 2006. High incidence of new sexually transmitted infections in the year following a sexually transmitted infection: a case for rescreening. *Ann Intern Med 145:* 564–572.
9. Minkoff H, Grunebaum AN, Schwarz RH, Feldman J, Cummings M, Crombleholme W, Clark L, Pringle G, McCormack WM, 1984. Risk factors for prematurity and premature rupture of membranes: a prospective study of the vaginal flora in pregnancy. *Am J Obstet Gynecol 150:* 965–972.
10. Cotch MF, Pastorek JG, Nugent RP, Hillier SL, Gibbs RS, Martin DH, Eschenbach DA, Edelman R, Carey JC, Regan JA, Krohn MA, Klebanoff MA, Rao AV, Rhoads GG, the Vaginal Infections and Prematurity Study Group, 1997. *Trichomonas vaginalis* associated with low birth weight and preterm delivery. *Sex Transm Dis 24:* 353–360.
11. Mann JR, McDermott S, Gill T, 2010. Sexually transmitted infection is associated with increased risk of preterm birth in South Carolina women insured by Medicaid. *J Matern Fetal Neonatal Med 23:* 563–568.
12. Moodley P, Wilkinson D, Connolly C, Moodley J, Sturm AW, 2002. *Trichomonas vaginalis* is associated with pelvic inflammatory disease in women infected with human immunodeficiency virus. *Clin Infect Dis 34:* 519–522.
13. Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N, Goeman J, Behets F, Batter V, Alary M, Heyward WL, Ryder RW, Piot P, 1993. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. *AIDS 7:* 95–102.
14. Laga M, Alary M, Nzila N, Monoka AT, Tuliza M, Behets F, Goeman J, St. Louis M, Piot P, 1994. Condom promotion, sexually transmitted diseases treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. *Lancet* 344*:* 246–248.
15. McClelland RS, Sangaré L, Hassan WM, Lavreys L, Mandaliya K, Kiarie J, Ndinya-Achola J, Jaoko W, Baeten JM, 2007. Infection with *Trichomonas vaginalis* increases the risk of HIV-1 acquisition. *J Infect Dis 195:* 698–702.
16. Van Der Pol B, Kwok C, Pierre-Louis B, Rinaldi A, Salata RA, Chen P-L, van de Wijgert J, Mmiro F, Mugerwa R, Chipato T, Morrison CS, 2008. *Trichomonas vaginalis* infection and human imunodeficiency virus acquisition in African women. *J Infect Dis 197:* 548–554.
17. Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, Kiarie J, Inambao M, Kilembe W, Farquhar C, Celum C, the Partners in Prevention HSV/HIV Transmission Study Team, 2012. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Infect Dis 205:* 358–365.
18. Wang CC, McClelland RS, Reilly M, Overbaugh J, Emery SR, Mandaliya K, Chohan B, Ndinya-Achola J, Bwayo J, Kreiss JK, 2001. The effect of treatment of vaginal infections on shedding of human immunodeficiency virus type 1. *J Infect Dis 183:* 1017–1022.
19. Kissinger P, Amedee A, Clark RA, Dumestre J, Theall KP, Myers L, Hagensee ME, Farley TA, Martin DH, 2009. *Trichomonas vaginalis* treatment reduces vaginal HIV-1 shedding. *Sex Transm Dis 36:* 11–16.
20. Homans J, Christensen S, Stiller T, Wang C-H, Mack W, Anastos K, Minkoff H, Young M, Greenblatt R, Cohen M, Strickler H, Karim R, Spencer LY, Operskalski E, Frederick T, Kovacs A, 2012. Permissive and protective factors associated with presence, level, and longitudinal pattern of cervicovaginal HIV shedding. *J Acquir Immune Defic Syndr 60:* 99–110.
21. Allsworth JE, Ratner JA, Peipert JF, 2009. Trichomoniasis and other sexually transmitted infections: results from the 2001–2004 national health and nutrition examination surveys. *Sex Transm Dis 36:* 738–744.
22. Weston TE, Nicol CS, 1963. Natural history of trichomonal infection in males. *Br J Vener Dis 39:* 251–257.
23. Krieger JN, 1993. Trichomoniasis in men: old issues and new data. *Sex Transm Dis 22:* 83–96.
24. Hobbs MM, Kazember P, Reed AW, Miller WC, Nkata E, Zimba D, Daly CC, Chakraborty H, Cohen MS, Hoffman I, 1999. *Trichomonas vaginalis* as a cause of urethritis in Malawian men. *Sex Transm Dis 26:* 381–387.
25. Stark JR, Judson G, Alderete JF, Mundodi V, Kucknoor AS, Giovannucci EL, Platz EA, Sutcliffe S, Fall K, Kurth T, Ma J, Stampfer MJ, Mucci LA, 2009. Prospective study of *Trichomonas vaginalis* infection and prostate cancer incidence and mortality: physicians' health study. *J Natl Cancer Inst 101:* 1406–1411.
26. Sutcliffe S, Neace C, Magnuson NS, Reeves R, Alderete JF, 2012. Trichomoniasis, a common curable STI, and prostate carcinogenesis: a proposed molecular mechanism. *PLoS Pathog 8:* e1002801.
27. Huppert JS, Mortensen JE, Reed JL, Kahn JA, Rich KD, Miller WC, Hobbs MM, 2007. Rapid antigen testing compares favorably with transcription-mediated amplification assay for the detection of *Trichomonas vaginalis* in young women. *Clin Infect Dis 45:* 194–198.
28. Nye MB, Schwebke JR, Body BA, 2009. Comparison of APTIMA *Trichomonas vaginalis* transcription-mediated amplification to wet mount microscopy, culture, and polymerase chain reaction for diagnosis of trichomoniasis in men and women. *Am J Obstet Gynecol 200: 188* e1–1e7.
29. Stoner KA, Rabe LK, Meyn LA, Hillier SL, 2013. Survival of *Trichomonas vaginalis* in wet preparation and on wet mount. *Sex Transm Infect 89:* 485–488.
30. Chapin K, Sndrea S, 2011. APTIMA® *Trichomonas vaginalis*, a transcription-mediated amplification assay for detection of *Trichomonas vaginalis* in urogenital specimens. *Expert Rev Mol Diagn 11:* 679–688.
31. Huppert JS, Mortensen JE, Reed JL, Kahn JA, Rich KD, Miller WC, Hobbs MM, 2007. Rapid antigen testing compares favorably with transcription-mediated amplification assay for the detection of *Trichomonas vaginalis* in young women. *Clin Infect Dis 45:* 194–198.
32. Jones HE, Lippman SA, Caiaffa-Filho HH, Young T, van de Wijgert JH, 2013. Perfomance of a rapid self-test for detection of *Trichomonas vaginalis* in South Africa and Brazil. *J Clin Microbiol 51:* 1037–1039.
33. Pearce DM, Styles DN, Hardick JP, Gaydos CA, 2013. A new rapid molecular point-of-care assay for *Trichomonas vaginalis*: preliminary performance data. *Sex Transm Infect 89:* 495–497.
34. Workowski KA, Berman SM, Centers for Disease Control and Prevention, 2010. Sexually Transmitted Diseases Treatment Guidelines, 2010. *Clin Infect Dis 53 (Suppl 3):* S59–S63.
35. Kirkcaldy RD, Augostini P, Asbel LE, Bernstein KT, Kerani RP, Mettenbrink CJ, Pathela P, Schwebke JR, Secor WE,

Workowski KA, Davis D, Braxton J, Weinstock HS, 2012. *Trichomonas vaginalis* antimicrobial drug resistance in 6 US cities, STD Surveillance Network, 2009–2010. *Emerg Infect Dis 18:* 939–943.
36. Kissinger P, Secor WE, Leichliter JS, Clark RA, Schmidt N, Curtin E, Martin DH, 2008. Early repeated infections with *Trichomonas vaginalis* among HIV-positive and HIV-negative women. *Clin Infect Dis 46:* 994–999.
37. Helms DJ, Mosure DJ, Secor WE, Workowski KA, 2008. Management of *Trichomonas vaginalis* in women with suspected metronidazole hypersensitivity. *Am J Obstet Gynecol 98:* 370 e1–e7.
38. Asensio T, Dávila I, Moreno E, Laffond E, Macías E, Ruiz A, Lorente F, 2008. Anaphylaxis due to metronidazole with positive skin prick test. *J Investig Allergol Clin Immunol 18:* 136–142.
39. Piskin G, Mekkes JR, 2006. Stevens-Johnson syndrome from metronidazole. *Contact Dermat 55:* 192–193.
40. Miller WC, Swygard H, Hobbs MM, Ford CA, Handcock MS, Morris M, Schmitz JL, Cohen MS, Harris KM, Udry JR, 2005. The prevalence of trichomoniasis in young adults in the United States. *Sex Transm Dis 32:* 593–598.
41. Munson E, Kramme T, Napierala M, Munson KL, Miller C, Hryciuk JE, 2012. Female epidemiology of transcription-mediated amplification-based *Trichomonas vaginalis* detection in a metropolitan setting with a high prevalence of sexually transmitted infection. *J Clin Microbiol 50:* 3927–3931.
42. Munson KL, Napierala M, Munson E, Schell RF, Kramme T, Miller C, Hryciuk JE, 2013. Screening of male patients for *Trichomonas vaginalis* with transcription-mediated amplification in a community with a high prevalence of sexually transmitted infection. *J Clin Microbiol 51:* 101–104.
43. Hoots BE, Peterman TA, Torrone EA, Weinstock H, Meites E, Bolan GA, 2013. A trich-y question: should *Trichomonas vaginalis* infection be reportable? *Sex Transm Dis 40:* 113–116.
44. Owusu-Edusei K Jr, Chesson HW, Gift TL, Tao G, Mahajan R, Ocfemia MC, Kent CK, 2013. The estimated direct medical cost of selected sexually transmitted infections in the United States, 2008. *Sex Transm Dis 40:* 197–201.
45. Quinlivan EB, Patel SN, Grodensky CA, Colin CE, Tien H-C, Hobbs MM, 2012. Modeling the impact of *Trichomonas vaginalis* infection on HIV transmission in HIV-infected individuals in medical care. *Sex Transm Dis 39:* 671–677.
46. Chesson HW, Blandford JM, Pinkerton SD, 2004. Estimates of the annual number and cost of new HIV infections among women attributable to trichomoniasis in the United States. *Sex Transm Dis 31:* 547–551.
47. Gaydos CA, Hsieh Y-H, Barnes M, Quinn N, Agreda P, Jett-Goheen M, Whittle P, Hogan T, 2011. *Trichomonas vaginalis* infection in women who submit self-obtained vaginal samples after internet recruitment. *Sex Transm Dis 38:* 828–832.
48. Gaydos CA, Barnes MR, Quinn N, Jett-Goheen M, Hsieh Y-H, 2013. *Trichomonas vaginalis* infection in men who submit self-collected penile swabs after internet recruitment. *Sex Transm Infect 89:* 504–508.
49. Lustig G, Ryan CM, Secor WE, Johnson PJ, 2013. *Trichomonas vaginalis* contact dependent cytolysis of epithelial cells. *Infect Immun 81:* 1411–1419.
50. Mann JR, McDermott S, Barnes TL, Hardin J, Bao H, Zhou L, 2009. Trichomoniasis in pregnancy and mental retardation in children. *Ann Epidemiol 19:* 891–899.
51. Klebanoff MA, Carey JC, Hauth JC, Hillier SL, Nugent RP, Thom EA, Ernest JM, Heine RP, Wapner RJ, Trout W, Moawad A, Leveno KJ, Miodovnik M, Sibai BM, Van Dorsten JP, Dombrowski MP, O'Sullivan MJ, Varner M, Langer O, McNellis D, Roberts JM; National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units, 2001. Failure of metronidazole to prevent preterm delivery among pregnant women with asymptomatic *Trichomonas vaginalis* infection. *N Engl J Med 345:* 487–493.
52. Helms DJ, Mosure DJ, Metcalf CA, Douglas JM, Malotte CK, Paul SM, Peterman TA, 2008. Risk factors for prevalent and incident *Trichomonas vaginalis* among women attending three sexually transmitted disease clinics. *Sex Transm Dis 35:* 484–488.
53. Peterman TA, Tian LH, Metcalf CA, Malotte K, Paul SM, Douglas JM, for the RESPECT-2 Study Group, 2009. Persistent, undetected *Trichomonas vaginalis* infections? *Clin Infect Dis 48:* 259–260.
54. Gatski M, Kissinger P, 2010. Observation of probable persistent, undetected *Trichomonas vaginalis* infection among HIV-positive women. *Clin Infect Dis 21:* 114–115.
55. Bosserman EA, Helms DJ, Mosure DJ, Secor WE, Workowski KA, 2011. Utility of antimicrobial susceptibility testing in *Trichomonas vaginalis*-infected women with clinical treatment failure. *Sex Transm Dis 38:* 983–987.
56. Hobbs MM, Lapple DM, Lawing LF, Schwebke JR, Cohen MS, Swygard H, Atashili J, Leone PA, Miller WC, Seña AC, 2006. Methods for detection of *Trichomonas vaginalis* in the male partners of infected women: implications for control of trichomoniasis. *J Clin Microbiol 44:* 3994–3999.
57. Price MA, Stewart SR, Miller WC, Behets F, Dow WH, Martinson FEA, Chilongozi D, Cohen MS, 2006. The cost-effectiveness of treating male trichomoniasis to avert HIV transmission in men seeking sexually transmitted disease care in Malawi. *J Acquir Immune Defic Syndr 43:* 202–209.
58. Carlton JM, Hirt RP, Silva JC, Delcher AL, Schatz M, Zhao Q, Wortman JR, Bidwell SL, Alsmark UC, Besteiro S, Sicheritz-Ponten T, Noel CJ, Dacks JB, Foster PG, Simillion C, Van de Peer Y, Miranda-Saavedra D, Barton GJ, Westrop GD, Müller S, Dessi D, Fiori PL, Ren Q, Paulsen I, Zhang H, Bastida-Corcuera FD, Simoes-Barbosa A, Brown MT, Hayes RD, Mukherjee M, Okumura CY, Schneider R, Smith AJ, Vanacova S, Villalvazo M, Haas BJ, Pertea M, Feldblyum TV, Utterback TR, Shu CL, Osoegawa K, de Jong PJ, Hrdy I, Horvathova L, Zubacova Z, Dolezal P, Malik SB, Logsdon JM Jr, Henze K, Gupta A, Wang CC, Dunne RL, Upcroft JA, Upcroft P, White O, Salzberg SL, Tang P, Chiu CH, Lee YS, Embley TM, Coombs GH, Mottram JC, Tachezy J, Fraser-Liggett CM, Johnson PJ, 2007. Draft genome sequence of the sexually transmitted pathogen *Trichomonas vaginalis*. *Science 315:* 207–212.
59. Conrad MD, Gorman AW, Schillinger JA, Fiori PL, Arroyo R, Malla N, Dubey ML, Gonzalez J, Blank S, Secor WE, Carlton JM, 2012. Extensive genetic diversity, unique population structure and evidence of genetic exchange in the sexually transmitted parasite *Trichomonas vaginalis*. *PLoS Negl Trop Dis 6:* e1573.
60. Hirt RP, 2013. *Trichomonas vaginalis* virulence factors: an integrative overview. *Sex Transm Infect 89:* 439–443.
61. Meade JC, Carlton JM, 2013. Genetic diversity in *Trichomonas vaginalis*. *Sex Transm Infect 89:* 444–448.
62. Goodhew EB, Secor WE, 2013. Drug library screening against metronidazole-sensitive and metronidazole-resistant *Trichomonas vaginalis* isolates. *Sex Transm Infect 89:* 479–484.
63. Helms DJ, Mosure DJ, Secor WE, Workowski KA, 2008. Management of *Trichomonas vaginalis* in women with suspected metronidazole hypersensitivity. *Am J Obstet Gynecol 198:* 370 e1–e7.
64. Muzny C, Barnes A, Mena L, 2012. Symptomatic *Trichomonas vaginalis* infections in the setting of severe nitroimidazole allergy: successful treatment with boric acid. *Sex Health 9:* 389–391.
65. Ratzan JJ, 1969. Monilial and trichomonal vaginitis. Topical treatment with povidone-iodine preparations. *Calif Med 110:* 24–27.
66. Waters LJ, Dave SS, Deayton JR, French PD, 2005. Recalcitrant *Trichomonas vaginalis* infection: a case series. *Int J STD AIDS 16:* 505–509.