

Trichomonas vaginalis Infection: The Most Prevalent Nonviral Sexually Transmitted Infection Receives the Least Public Health Attention

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(See the article by Seña et al. on pages 13–22)

Trichomonas vaginalis infection was first described as a venereal disease in the mid-20th century, decades before *Chlamydia trachomatis* infection would be recognized as such. The motile protozoan responsible for trichomoniasis in women is easily viewed with unsophisticated microscopy. Unfortunately, this leads to the impression that, because these organisms are large, motile, and easily seen, wet preparation microscopy is highly sensitive. This ignores the high organism load necessary for vaginal sampling to capture organisms. Because wet preparations with positive results are obtained from women with high organism loads, it is not surprising that the majority of these women are symptomatic. As a result of this, asymptomatic women are rarely tested outside of sexually transmitted infection (STI) clinic settings. Since the development of nucleic acid amplification tests for *T. vaginalis* DNA, our understanding of the epidemiology of this pathogen has improved and suggests that as many as one-third of infections in women may be asymptomatic.

T. vaginalis infection is the most prevalent nonviral STI, both in the United States and globally. The World Health Organization estimates that its prevalence ranges from 170 million to 190 million cases worldwide each year (the estimated prevalence in the United States is ~8 million cases per year). These estimates are based

on the assumption of wet mount sensitivity ranges from 60% to 80%. This suggests that the estimates may, in fact, be low, given that the probable sensitivity for wet mount microscopy is probably closer to 35%–60% [1–5]. However, even if we take these estimates at face value, why is so little attention paid to the fact that the prevalence of *T. vaginalis* infection is equal to the combined estimates for the prevalence of *C. trachomatis* and *Neisseria gonorrhoeae* infection?

The relative proportion of these estimates is supported by data from a variety of populations [1, 6, 7]. In a Midwestern obstetrics clinic that routinely screens for all 3 of these STIs during the first trimester of pregnancy, the prevalences of *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* infection for mid-2004 through mid-2006 were 3.0%, 0.9%, and 3.9%, respectively (James A. Williams, personal communication). Among 186 female STI clinic attendees in Marion County, Indiana, the prevalences of *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* infection in a convenience sample from the mid-1990s were 15.1%, 9.1%, and 22.0%, respectively [2]. In the same study, the prevalences for a convenience sample of male STI clinic attendees were 5.4%, 5.2%, and 5.0%, respectively. Although the prevalence of *T. vaginalis* infection among men was low in this study, the prevalences of *C. trachomatis* and *N. gonorrhoeae* infection were also low for an STI clinic population. Other studies have measured the prevalence of *T. vaginalis* infection in men [8–12] and have found that *T. vaginalis* is a common pathogen, although infection is less prevalent among men than among women. Men with *T. vaginalis* infection are predominantly asymptomatic. This low level of clinical manifestation among men leads to reduced emphasis on case

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finding, because the limited resources available are directed toward agents that cause urethritis and related syndromes.

Given the high prevalence of disease relative to other STIs in various populations of women, why is *T. vaginalis* infection not included in aggressive screening and control programs? One argument has been that *T. vaginalis* infection is essentially a self-clearing nuisance. However, longitudinal sampling demonstrates that, without treatment, infection can persist for at least 3 months [3]. Furthermore, *T. vaginalis* infection has been associated with reproductive tract sequelae, including pelvic inflammatory disease and adverse outcomes of pregnancy [13–15]. It is worth noting that not only is the prevalence of infection lower among men than among women, but men also rarely experience consequences of untreated infection. Perhaps this is the population for whom this is a nuisance disease and, therefore, an insignificant pathogen.

If the reproductive health consequences of *T. vaginalis* infection in women are insufficient to warrant public health control efforts, then perhaps increased transmission of HIV should generate interest in this endemic pathogen. Although the role, if any, of *C. trachomatis* as a cofactor in HIV acquisition is unclear, *N. gonorrhoeae* has been associated with increased risk of HIV infection in both men and women. However, of these 3 discharge-causing STIs, *N. gonorrhoeae* infection is the least prevalent. *T. vaginalis* infection has also been shown to be associated with increased odds of HIV acquisition in female sex workers [6] and family planning clinic attendees [16] in East and southern Africa. Although the adjusted ORs for acquisition of HIV infection in women with *T. vaginalis* are lower than the ORs for women infected with *N. gonorrhoeae*, the prevalence is as much as 3 times as high, potentially making *T. vaginalis* infection the more important STI to target for control programs. *T. vaginalis* has also been shown to be associated with increased viral load in the seminal and the cervicovaginal compartments [17, 18]. Because viral load is the largest risk factor for transmission of HIV within couples with discordant infection status, this suggests that control of *T. vaginalis* infection in men may help reduce the infectivity of HIV-infected persons.

Although most of the information I have presented here is not new, when considered in its entirety, the information regarding the prevalence and potential consequences of *T. vaginalis* infection among both men and women demands attention. Members of the STI field must become advocates for improving the availability of resources for *T. vaginalis*-control efforts. This is not the first call to action regarding this pathogen; several leaders in the STI field have raised this issue elsewhere [19–21].

We need to apply the lessons we have learned from *C. trachomatis*-control programs to effectively reduce the burden of disease, which predominately involves women. One of the most important issues is that, when controlling STIs, partners matter.

In the important study by Seña et al. [22] in this issue of the journal, an extensive evaluation of male partners of *T. vaginalis*-infected women was undertaken. The relevance of this type of study is 3-fold: (1) demonstrating that men are susceptible to *T. vaginalis* infection increases practitioner awareness, (2) understanding the concordance in dyads emphasizes the need to manage partners, and (3) understanding the clinical manifestations helps target diagnostic and treatment efforts.

Previous studies of *C. trachomatis* infection have shown concordance within dyads [23–25] to be similar to the rates shown by Seña et al. [22] for *T. vaginalis* infection, making it reasonable to apply findings from chlamydia-control programs to the issue of *T. vaginalis* control. Data from a variety of sources have shown that focusing attention only on screening and treating women for *C. trachomatis* has not achieved the desired sustainable reductions in prevalence [26–28]. Untreated partners continue to be a source of reinfection that needs to be addressed. Rather than focusing on contact tracing to identify and treat infected men, screening for *T. vaginalis* needs to be included in developing programs for the screening of asymptomatic men for *C. trachomatis* and *N. gonorrhoeae*.

Including screening for *T. vaginalis* in STI-control programs should not be limited to men; increased testing of asymptomatic women is necessary to identify those infections that may persist in the absence of physical signs that may prompt women to seek health care. Addition of *T. vaginalis* to existing and developing screening programs is increasingly feasible, because both point-of-care and nucleic acid amplification assays are now available for use in routine settings. Because *T. vaginalis* infection is easily treated, more epidemiologic studies (such as the one by Seña et al. [22]) are needed to guide treatment in settings where diagnostic testing is not feasible, particularly for men. We need to encourage the STI diagnostic industry to continue development of improved assays, but this is unlikely to become a priority in the absence of national mandates for testing. In the meantime, testing for *T. vaginalis* using any method is better than performing no diagnostic examinations and relying solely on signs and symptoms. However, even simple diagnostic tests and treatment require resources directed toward controlling this pathogen. Without specifically targeted funding, infection with *T. vaginalis* will continue to be a “silent” STI, placing millions of women at increased risk of reproductive health complications and HIV infection.

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