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Trichomonas: Clinical Analysis of a Highly Prevalent and Misdiagnosed Infection

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INTRODUCTION

Trichomoniasis, an infection caused by the protozoan parasite *Trichomonas vaginalis* (TV), is a widespread sexually transmitted disease (STD) that affects men and women, though infection is more common in women.[1] Typical infection sites are the lower genital tract (vagina, urethra, or vulva) in women and the urethra in men, enabling the parasite to be transmitted through penis-to-vagina intercourse or vulva-to-vulva contact with an infected partner.

An estimated 7.4 million new cases of trichomoniasis occur annually in the United States, making it more common than infections from human papillomavirus (HPV; 6.2 million), herpes simplex virus (1.5 million), *Chlamydia trachomatis* (CT; 3.5 million), and *Neisseria gonorrhoeae* (NG; 700,000).[2,3] Not only is trichomoniasis the most prevalent non-viral STD in the United States (Figure 1), it is also one of the most curable.[4] Yet, despite the estimated high prevalence and treatability, trichomoniasis is still not classified as a "reportable disease," and TV infections are not routinely reported to the Centers for Disease Control and Prevention (CDC).[4,5] Because it is not part of routine screening, its prevalence and incidence are likely underestimated.[3]

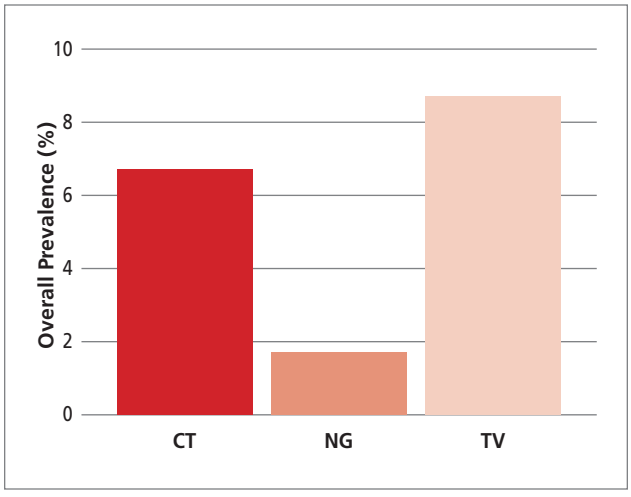

FIGURE 1. Prevalence of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV) infections in US Women Undergoing CT/NG Screening. Data from Ginocchio et al.[4]

Health Risks of Trichomoniasis

Untreated TV infections may result in long-term sequelae, such as pelvic inflammatory disease, pre-term births, premature rupture of membranes, infants with low birth weight, and post-abortion or post-hysterectomy infection.[4-6] There is also a risk of tubal infertility and increased incidence of human immunodeficiency virus (HIV) transmission.[5-8]

To prevent these negative health outcomes, it is critical to correctly diagnose and treat TV infection.[4] At present, the most commonly used diagnostic test, wet mount microscopy, has several limitations including very low sensitivity for TV, representing a barrier to effective diagnosis and treatment of trichomoniasis.[3,9]

Signs and Symptoms

TV infection may be asymptomatic in as many as 50% of women, persist for months to years, or be part of a mixed infectious process with other STDs or genitourinary infections, adding to the challenge of a clear diagnosis.[3] Additionally, the clinical signs and symptoms of trichomoniasis are not unique.

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TABLE 1. Sensitivity Comparison of Diagnostic Tests for *Trichomonas vaginalis* Infection

Test Method	Range of Sensitivity
APTIMA TV assay	95-100%[8]
OSOM® Trichomonas	62-95%[3]
Affirm™ VPIII	44-83%[3]
Culture	38-82%[6]
Wet mount	55-60%[3,7]
Pap smear	< 25-60%[2,3,9]

When symptoms are present, usually within 5 to 28 days after exposure, they can range from mild irritation to severe inflammation and may resemble urethritis, vaginitis, or cervicitis.[1,3] Symptomatic women typically have a diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation, which may be confused with bacterial vaginosis.[8]

TESTING: THE CHANGING LANDSCAPE

Diagnosis of trichomoniasis is not possible based on symptoms alone; it requires a physical examination and a laboratory test.[1] There are currently no published testing guidelines for TV, nor criteria to determine which patients should be screened.[2,7] Laboratory tests for TV have varying levels of sensitivity, specificity, and practicality in the clinical setting, and some may be especially variable in asymptomatic patients (Table 1).

Comparison of Diagnostic Tests

Wet mount microscopy of vaginal fluid has high specificity for TV but low sensitivity (55%-60%).[3,7] Moreover, microscopy must be performed within 20 minutes of sample collection to assess organism motility, and the sensitivity is highly dependent on the experience of the microscopist, conditions of specimen transport to the laboratory, and whether patients are symptomatic or asymptomatic.[3] Additionally, microscopy is not a sensitive tool for differentiating TV from *Pentatrichomonas hominis*, a nonpathogenic gastrointestinal flagellate that may contaminate samples during collection.[4] Despite its imperfect performance, wet mount remains the most frequently used diagnostic test for TV because it is rapid, inexpensive, and widely available in STD clinics.[3,9]

Pap smears are unreliable for diagnosing trichomoniasis since they have been shown to have low sensitivity for TV (< 25%-60%) and a 4% to 8% rate of false positives.[2,3,9]

Up to now, culture has been considered the gold standard TV test because of its superior sensitivity over both wet mount microscopy and the OSOM test discussed below.[7] Its use is limited, however, because it requires immediate inoculation into the media, proper incubation conditions, frequent microscopic examinations, and several days for completion.[6,7] Culture can also be costly and has varying sensitivity (38%-82%[6]) due to difficulty visualizing low numbers of organisms, reducing its suitability for routine clinical use.[4,6]

Two FDA-approved point-of-care tests—Affirm™ VPIII (Becton Dickinson, CA) and OSOM® *Trichomonas* Rapid Test (Genzyme Diagnostics, MA)—are more sensitive than wet mount microscopy, but their use is limited to vaginal specimens from symptomatic patients.[3,7] Affirm is a DNA hybridization probe test designed to differentiate pathogens associated with bacterial vaginosis (*Gardnerella vaginalis*) and vaginitis (TV and *Candida* species).[5] OSOM is an immunochromatographic assay that produces results within 20 minutes in the clinic, whereas Affirm (which takes about 1 hour) is usually performed in a laboratory.[3] Both tests are interpreted subjectively by a color change on the test pad.

The sensitivities of Affirm and OSOM outperform that of wet mount in symptomatic patients but are much lower in asymptomatic patients, so these tests are not appropriate for screening.[3] One study found that Affirm produced several false-negative results (15 out of 41 specimens), increasing the chance that patients may be misdiagnosed and treated for the wrong etiology or treated with a less-than-optimal regimen.[5] This could lead to recurrence of symptoms, continued transmission of TV, and development of treatment resistance. The lack of sensitivity in clinically differentiating between vaginosis and vaginitis supports the need to have a definitive test for TV.[5]

Diagnostic assays based on nucleic acid amplification (NAA), either by polymerase chain reaction (PCR) or transcription-mediated amplification (TMA), are generally more sensitive than non-amplified assays, such as Affirm or OSOM.[3] NAA tests (NAATs) combine excellent performance with a more rapid turnaround time than culture.[7]

The only FDA-approved NAAT for trichomoniasis is the APTIMA TV assay (Gen-Probe Inc, CA). Sample types include clinician-collected endocervical swabs (CES), clinician-collected vaginal swabs (CVS), urine specimens, and specimens collected in PreservCyt (PCyt) Solution (Hologic Inc, MA) for liquid-based cytology.[4,6] APTIMA has been shown to maintain its high sensitivity regardless of sample type. A multicenter study showed that the sensitivity of the APTIMA TV assay was 95% for urine and 100% for CVS, CES, and PCyt samples.[8] This test is offered by laboratories as a stand-alone test and in some of the newer, more sensitive vaginitis panels, such as LabCorp's NuSwab® profiles.

Implications of New Testing Methods

NAATs have changed the diagnostic landscape for STDs and are now the standard of care for CT and NG testing.[7] The APTIMA assay for CT/NG testing has high analytic sensitivity,

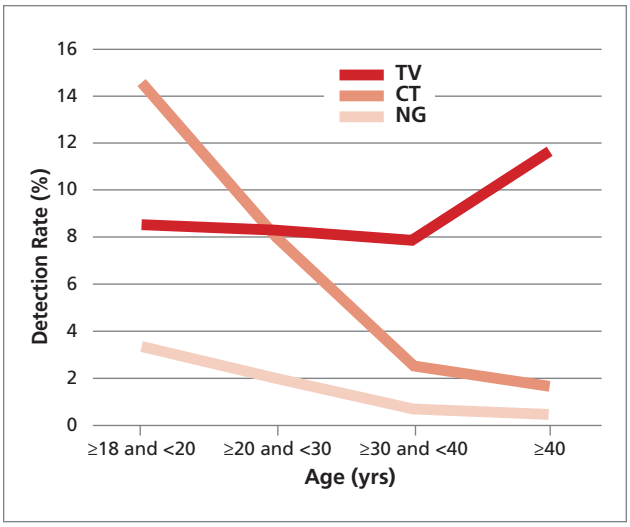

FIGURE 2. Prevalence of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV) by age in 7,593 US women screened for CT/NG. Data from Ginocchio et al.[4]

low inhibition rates, and can use various specimen types. Similarly, the APTIMA TV assay is expected to improve diagnostic accuracy for TV. Side-by-side comparisons have shown that the APTIMA TV assay has greater sensitivity than other methods (see Table 1). Owing to this lower risk of false negatives, the APTIMA assay may be considered for patients at risk for TV infection who have negative wet mount results.[7]

This and other similar studies have identified an unexpectedly high prevalence of trichomoniasis among middle-aged women who might not be part of the normal screening group for STDs (Figure 2).[4,5] In one study, TV prevalence was significantly higher than CT or NG prevalence among patients older than age 30.[4] Another study showed similar results in which 36- to 45-year-old women had no CT or NG infections but significantly more TV infections than the 16- to 25-year-olds.[5] TV is unique among STDs in its significant association with age groups greater than 30 years.[3] The high prevalence in all age groups, however, suggests that all women at risk for STDs should be screened for TV, whether or not they are also being screened for CT or NG.[4]

High prevalence in asymptomatic women also emphasizes the need for the CDC to classify TV as a reportable disease.[4] There are no published screening recommendations for TV, except in the case of specific risk factors (eg, pregnancy). Interestingly, many sequelae of untreated TV infection are similar to those that prompted screening recommendations for CT and NG in the past decade.[3] The efficiency of the APTIMA TV assay provides hope that TV screening and reporting may become more common. For example, TV testing could become part of routine HPV/cytology screening since APTIMA can be performed on either the same PCyt sample or another simple swab sample.[4] APTIMA is also sensitive enough in urine to allow patients to self-collect samples, increasing the convenience of screening large populations.[3] See Table 2 for TV testing recommendations.

TREATMENT

Effective and inexpensive antibiotic therapy for TV infection is available, and prompt treatment may prevent disease transmission and complications.[8] Common treatments are metronidazole or tinidazole, given by mouth in a single dose. Metronidazole can be used by pregnant women.[1] These antibiotics treat existing TV infections, but patients are susceptible to reinfection with continued exposure to the parasite. Couples should be treated simultaneously, and they should avoid sex until they complete treatment.[1]

CONCLUSION

Trichomoniasis is under-recognized by both health care providers and patients; neither is aware of its predominance

TABLE 2. Considerations for *Trichomonas vaginalis* (TV) Testing

Patient Population	Testing Recommendation
All women at risk for sexually transmitted diseases (STDs)	Screen for TV infection, whether or not they are also screened for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG).[4]
Women at risk for TV infection who have negative wet mount results	APTIMA TV assay should be considered to confirm test results.[7]
Women at risk for TV infection who do not exhibit any symptoms	APTIMA TV assay has been shown to be the most sensitive TV test, even in asymptomatic women.[3,5]
Middle-aged women who might not be part of the normal screening group for STDs	Screen for TV infection in addition to CT and NG.[4,5]

Clinician Experience

Dr Gerald E. Pass at New Horizons Casa Grande, an ObGyn medical practice in Arizona that serves 600 women in the greater Phoenix area per month, has been ordering the NAAT for *Trichomonas vaginalis* for 2 years now (NuSwab® from LabCorp), and he uses the test because of the recurrent visits from patients who had previously tested negative for chlamydia and gonorrhea infection. Dr Pass says, "Many times I find that the infections we are diagnosing are due to Trichomonas, even in relatively asymptomatic patients. It is important to keep a high index of suspicion for Trichomonas when screening for sexually transmitted diseases."

Dr Yolanda K. Vaughan, who is a staff physician at Inova Fairfax Hospital in Richmond, Virginia, switched from microscopy to NAAT (NuSwab® from LabCorp) to diagnose *Trichomonas vaginalis* infection. Dr Vaughan typically sees approximately 100 patients per week and says, "I am a former medical technologist, so the microscope was like my right hand, and I used the microscope to diagnose Trichomonas exclusively," says Dr Vaughan. "Now, I use NuSwab instead because I am able to detect the infection in asymptomatic patients as well and," she continues, "NuSwab also decreases the need for additional office visits, which is convenient for my patients, and helps to detect other sexually transmitted diseases."

How to Get the APTIMA TV Test

It is important for clinicians to understand what technology is used in TV tests. LabCorp offers the APTIMA TV assay because of its superior performance, and makes it convenient for clinicians by accepting specimens from liquid-based pap vials, urine samples, and in profiles using vaginal swabs like NuSwab® VG, which differentiates bacterial vaginosis, candidiasis, and TV infection. For more information visit www.labcorp.com or ask your local sales representative.

among STDs or the significant sequelae of untreated infection, especially HIV acquisition and adverse pregnancy outcomes.[3] This lack of awareness is likely due to the unreliability of traditional diagnostic tests and the fact that trichomoniasis is not a "reportable" disease. The combination of high prevalence, ease of transmission, availability of effective and inexpensive treatment, and significant health risks and costs of untreated infection creates a strong public health motivation to screen patients for TV infection.

Although wet mount microscopy is commonly used due to its wide availability, low cost, and rapid results, it is one of the least sensitive TV tests available.[3,9] Culture is another standard test for detecting the parasite, but it can be costly, time consuming, and only moderately sensitive.[4] The two non-culture, non-amplified tests, Affirm and OSOM, are more sensitive than wet mount microscopy but are limited to vaginal specimens from symptomatic patients, since sensitivity is too low in asymptomatic patients or other sample types.[3]

NAA testing, which combines high performance with more rapid turnaround than culture, has already become the standard of care for detection of CT and NG.[7] The approved NAAT TV assay, which has higher diagnostic accuracy than traditional methods, is poised to become the standard of care for TV detection as well.[7] This NAAT assay is the only assay that maintains high sensitivity even in asymptomatic patients, and its performance has been shown to be consistent regardless of age or geographic location, adding to its utility for screening.[3,8]

References

1. Centers for Disease Control and Prevention. Sexually Transmitted Diseases (STDs): Trichomoniasis — CDC Fact Sheet. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2011. Available at: http://www.cdc.gov/std/trichomonas/STDFact-Trichomoniasis.htm. Accessed July 10, 2012.
2. Vaginitis. ACOG Practice Bulletin No. 72. Washington, DC: American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2006;107:1195-1206.
3. Chapin K, Andrea S. APTIMA® Trichomonas vaginalis, a transcription-mediated amplification assay for detection of Trichomonas vaginalis in urogenital specimens. E*xpert Rev Mol Diagn.* 2011;11(7):679-688.
4. Ginocchio CC, Chapin K, Smith JS, et al. Prevalence of Trichomonas vaginalis and coinfection with Chlamydia trachomatis and Neisseria gonorrhoeae in the United States as determined by the APTIMA® Trichomonas vaginalis Nucleic Acid Amplification Assay. *J Clin Microbiol.* 2012;doi:10.1128/JCM.00748-12.
5. Andrea SB, Chapin KC. Comparison of Aptima Trichomonas vaginalis transcription-mediated amplification assay and BD Affirm VPIII for detection of T. vaginalis in symptomatic women: performance parameters and epidemiological implications. *J Clin Microbiol.* 2011;49(3):866-869.
6. APTIMA® Trichomonas vaginalis Assay [Prescribing Information]. San Diego, CA: Gen Probe, Inc.; 2011.
7. Nye MB, Schwebke JR, Body BA. 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.* 2009:188.e1-188.e7.
8. Schwebke JR, Hobbs MM, Taylor SN, et al. Molecular testing for Trichomonas vaginalis in women; results from a prospective U.S. clinical trial. *J Clin Microbiol.* 2011;49(12):4106-4111.
9. Wendel KA, Erbelding EJ, Gaydos CA, Rompalo AM. Trichomonas vaginalis polymerase chain reaction compared with standard diagnostic and therapeutic protocols for detection and treatment of vaginal trichomoniasis. *Clin Infect Dis.* 2002;35(5):576-580.