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ORIGINAL ARTICLE

Trichomonas vaginalis AND HIV INFECTION: RELATION AND PREVALENCE AMONG WOMEN IN SOUTHERN BRAZIL

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ABSTRACT

Trichomoniasis is a curable sexually transmitted infection (STI) that has been reported to be linked to exposure to human immunodeficiency virus (HIV), although few studies have described this association. The purpose of this study was to focus on the incidence of trichomoniasis in low-income women, its relation to HIV status, viral load levels and TCD4$^+$ cell counts, among other risk factors, using an *in vitro* culture as a diagnostic test. A cross-sectional study among 267 women (103 HIV-positive and 164 HIV-negative) was conducted in 2015. The overall prevalence of *Trichomonas vaginalis* (TV) infection was 6.4%. Among HIV-positive and HIV-negative women, the prevalence was 3.9% and 7.9%, respectively, yet these results were not statistically different (p=0.1878). The factors associated with TV infection were cigarette smoking (OR= 3.52), vaginal itching (OR=4.43) and bacterial vaginosis (BV) (OR= 5.29). HIV status, TCD4$^+$ cell count and viral load were not associated with TV infection in this group. The prevalence rates found, lower than those observed in other studies, may be due to the fact that the women evaluated in the present study are part of a low-risk population as well as the limited sample size of HIV positive women.

KEY WORDS: Trichomoniasis; HIV infection; risk factors; sexually transmitted infections; protozoan diseases; *Trichomonas vaginalis*.

INTRODUCTION

Trichomonas vaginalis (TV) is a sexually transmitted protozoan, which causes trichomoniasis. This infection, which is related to low socioeconomic conditions, is rapidly and easily treated, answering for almost half of the curable sexually transmitted infections in the world (Rughooputh & Greenwell, 2005).

The most recent global estimates of curable sexually transmitted infection (STIs) report 143 million new cases of trichomoniasis per year.

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Among women and men aged 15-49, the overall prevalence was 5.0% and 0.6%, respectively (Newman et al., 2015). In Brazil, the prevalence of TV infection ranges from 1.9% to 37.5%, depending on the techniques used in the diagnosis as well as the population studied (Bravo et al., 2010).

Trichomoniasis is the most common non-viral sexually transmitted infection (STI), affecting both men and women, and may remain subclinical for long periods. In symptomatic patients, TV infection usually causes irritation and inflammation, malodor, itching and the classic green discharge, purulence and froth (Lewis, 2010). Women may also report dysuria, pelvic pain, dyspareunia, edema, vulvar erythema and occasionally a 'strawberry cervix'. Other complications of TV infection were associated with infertility, HIV transmission and, during pregnancy, premature rupture of membranes, preterm birth and low birth weight (Alves et al., 2011).

Since the beginning of the AIDS (acquired immunodeficiency syndrome) epidemic in the 1980s, sexually transmitted infections (STI) have been considered among the most common public health issues in the world. In both sexes, STIs may expose the organism to other diseases, including AIDS. It is estimated that every year 500 million people become infected with some curable STI (gonorrhea, chlamydia, syphilis and trichomoniasis) (Brasil, 2015).

TV infection has been playing a critical and little discussed role in HIV transmission (Sorvillo et al., 2001). Several studies have reported that certain STIs directly affect the transmissibility of HIV and may influence antiretroviral treatment and the consequent progression to AIDS as previously reviewed (Chun et al., 2013). STIs act as cofactors for HIV acquisition both for previously infected individuals that are potentially more infective and for uninfected individuals that show increased susceptibility (Wang et al., 2001).

It is also reported that in many cases trichomoniasis is considered bidirectional, since, in addition to TV infection enhancing exposure to HIV, women with other STIs have elevated viral shedding, potentially transmitting HIV under these conditions (Van Der Pol et al., 2008).

While in some women trichomoniasis is asymptomatic, in others, the infection induces a severe epithelial alteration (Mirmonsef et al., 2012). In these cases, the main mechanisms by which the TV infection exposes an individual to the risk of acquiring HIV are: stimulation of the inflammatory response in vaginal, exocervical and urethral epithelia; discontinuation of the epithelial barrier; recruitment of HIV target cells, such as $TCD4^{+}$ lymphocytes and macrophages; and production of micro hemorrhages. This imbalance can lead to the development of bacterial vaginosis or changes in the normal microbiota, essential for the acquisition of sexually transmitted diseases (Chun et al., 2013).

The protozoan can be an important co-factor in the spread and amplification of HIV transmission, because the inflammatory response produced by TV induces a large infiltration of leukocytes, affecting $TCD4^+$ cell and macrophages, target cells that are invaded by HIV (Sorvillo et al., 2001; Muzny et al., 2013).

The purpose of this study was to describe the incidence of trichomoniasis in low-income women, the relationship with HIV infection and other risk factors involved, using *in vitro* culture as a diagnosis.

MATERIALS AND METHODS

Study population

A cross-sectional study was conducted between January and December 2015, with patients who were seen at the Gynecology and Obstetrics Outpatient Clinic of the Maternal and Child Health Department- Medical School, UFPel. 267 samples of vaginal contents were collected, 164 from HIV seronegative women and 103 HIV seropositive. The samples were processed in the Laboratory of Parasitology at the Biology Institute of the same university. The patients who accepted to participate in the study were interviewed to obtain socioeconomic, behavioral and risk data, through a structured epidemiological questionnaire applied by the researchers.

Sample collection and laboratory procedures

During the gynecological examination, a vaginal swab was collected from each patient and *in vitro* cultures were performed in Diamond's TYM (Trypticase-Yeast extract-Maltose) medium (Diamond, 1957). Samples were analyzed daily for 5 days. After centrifugation at 202g for 10 min. aliquots of the pellet were analyzed microscopically using sterile pasteur pipettes for mobile trophozoites. The diagnosis of bacterial vaginosis (BV) was established by Gram staining and Nugent's score (Nugent et al., 1991). Complementary laboratory data ($TCD4^+$ count and viral load) of seropositive HIV patients were obtained from their medical records.

Statistical analysis

A descriptive analysis was carried out of the sample characteristics of both groups. We used the chi-square test and Fisher's exact test to compare significant differences between risk factors with TV infection.

Variables with $p<0.25$ were entered into a logistic regression through a multivariate model. Differences were considered statistically significant when $p \leq 0.05$. Odds Ratio (OR) was calculated with a confidence interval of 95%. All analyses were conducted using Statistix 9.0.

Ethical aspects

This study was approved by the Ethics Committee at the Federal University of Pelotas (Committee approval number 873.180). All study participants signed informed consent terms.

RESULTS

267 women from the city of Pelotas and region were screened for TV infection at the UFPel Obstetrics and Gynecology Outpatient Clinic. The study population consisted mainly of women with a mean age of 38 years (14 to 84 years), white (70%), low schooling including illiteracy (55.4% up to 8 years of schooling), low income (89.05% lower than the minimum wage), 22.5% pregnant and 38.6% HIV positive women.

The results of the bivariate analysis in the association of possible risk factors and TV infection are shown in table 1. At this stage of the analysis, the statistically significant socio-demographic factors found were non-white ethnicity ($p = 0.1118$) and married women ($p = 0.0975$). Among the behavioral factors, the use of cigarettes and alcohol and the irregular use of condoms were also significant in the univariate analysis. In an adjusted multivariate analysis (Table 2), the factors that had a statistically significant association with trichomoniasis infection were smoking ($p = 0.0183$), vaginal itching ($p= 0.0060$) and bacterial vaginosis ($p=0.0513$).

The main symptoms reported by infected patients were vaginal discharge, itching and malodor (Figure). On the other hand, we found that 17.9% of the infected women were asymptomatic.

The prevalence of TV infection in HIV-positive patients was 3.9% (4/103) and in HIV-negative was 7.9% (13/164), yet with no statistically significant difference between the groups ($p = 0.1878$). Most women in the HIV-positive group were characterized by $TCD4^+$ cell count >500 (62.4%) and undetectable viral load (64.4%). Of the 103 HIV-positive patients, only 15 (14.6%) presented AIDS, with $TCD4^+$ cell count < 200, and the prevalence of TV infection in this group was 6.7%, still lower than among HIV-negative women.

Table 1. Association (p <0.25) of *Trichomonas vaginalis* infection with demographic, behavioral and clinical characteristics of women attending the Gynecology Outpatient Clinic, Pelotas, 2015.

Variable	Total of women (n = 267)		TV positive† (n = 17)		p-Value*
	n	%	n	%	
Skin color					
White	187	70.0	9	4.8	
Other	80	30.0	8	10.0	0.1118
Marital status					
Married/living together	175	65.5	8	4.6	0.0975
Single/separated/ divorced/widowed	92	34.5	9	9.8	
Smoking					
Yes	95	35.6	10	10.5	0.0386
No	172	64.4	7	4.1	
Alcohol use past 30 days					
Yes	37	13.9	5	13.5	0.0551
No	230	86.1	12	5.2	
Regular condom use					
Yes	134	50.2	6	4.5	
No	133	49.8	11	8.2	0.2044
HIV positive					
Yes	103	38.6	4	3.9	0.1878
No	164	61.4	13	7.9	
Vaginal itching					
Yes	58	21.7	8	13.8	0.008
No	209	78.3	9	4.3	
Vaginal discharge					
Yes	132	49.4	12	9.1	0.0715
No	135	50.6	5	3.7	
Malodor					
Yes	55	20.6	6	10.9	0.1216
No	212	79.4	11	5.1	
Bacterial vaginosis‡					
Yes	10	3.7	2	20	0.0308
No	257	96.3	15	5.8	

TV: *Trichomonas vaginalis*; n: number of patients. * p-Value for the chi-square test using a significance level of 5%. † Diagnosis by *in vitro* culture. ‡ Diagnosis by Nuggent Criteria

Table 2. Association (p <0.05) of risk factors for *Trichomonas vaginalis* infection in women attended at the Gynecology Outpatient Clinic, southern Brazil (n = 267).

Variable	Total of women (n=267)		TV positive (n=17)		Multivariate analysis		
	n	%	n	%	OR	95% CI	p-Value
Smoking							
Yes	95	35.6	10	10.5	3.57	3.29 – 8.15	0.0183
No	172	64.4	7	4.1			
Vaginal itching							
Yes	58	21.7	8	13.8	4.43	2.29 – 7.21	0.0060
No	209	78.3	9	4.3			
Bacterial vaginosis							
Yes	10	3.7	2	20	5.29	1.71 – 6.91	0.0513
No	257	96.3	15	5.8			

OR, Odds Ratio; CI, Confidence interval

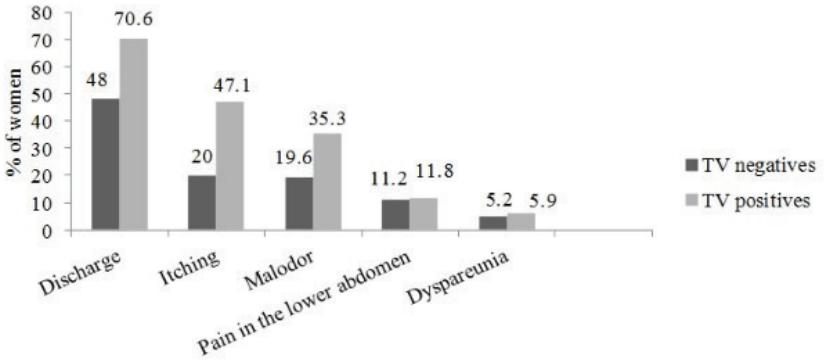

Figure. Comparative frequency of symptoms in patients infected by *Trichomonas vaginalis* at the Outpatient Clinic of Gynecology, southern Brazil, 2015.

DISCUSSION

The socio-demographic profile of the studied population, with low schooling and income rates, is due to the fact that the study was carried out in a public outpatient clinic. The low level of schooling associated with the high level of ignorance about the disease, suggests that lack of education reduces the awareness of risk and the ability to encourage their partners to use condoms (Grama et al., 2010).

Socioeconomic, demographic, behavioral and laboratory factors are strongly related to the prevalence found. Regarding the significant predictors of TV infection found in the crude analysis, these were also observed in other studies (Landers et al., 2004; Mason et al., 2005; Klinger et al., 2006; Barcelos et al., 2008, Leon et al., 2009; Alves et al., 2011; Grama et al., 2013).

The risk factors statistically associated with TV infection by multivariate analysis were: smoking, vaginal itching and bacterial vaginosis. Smoking was also associated with the acquisition of *T. vaginalis* in other studies (Grama et al., 2013; Swartzendruber et al., 2014). The strong association between smoking and the acquisition of sexually transmitted infections has been reported since smoking affects the immune system through cellular and humoral alterations, as well as reducing the circulating immunoglobulins, antibody response and phagocytic activity, which can directly influence the vaginal environment (Furber et al., 2007). In this study, we found that smoking increases the chances of infection up to 3.57 times.

Women with symptomatic trichomoniasis usually present vaginal itching as a result of the infection. In this study, this symptom was found in 47.1% of those infected with *T. vaginalis*, and 4.43 times more common in infected women. A study carried out in Northern Tanzania reported that women with vaginal itching have an increased odds (OR 1.77) of having TV (Klinger et al., 2006).

The presence of bacterial vaginosis in our study increased the chance of having TV, with an OR of 5.29. Similar results were verified in another study, highlighting a strong association between those two infections. Among the infections of the female genital tract, the most prevalent co-infection occurs between trichomoniasis and bacterial vaginosis (Landers et al., 2004).

Regarding the studied clinical signs among women infected by the protozoan, we found that 17.6% were asymptomatic. This rate, although inferior to that found in other studies, is worrying since due to the absence of symptoms many patients remain undiagnosed and are likely to infect other people. Most men remain asymptomatic after being infected with TV (Lewis, 2010). In addition to not seeking medical attention, they are vulnerable to a number of infections caused by different agents. Other authors report that asymptomatic infection can occur between 10% and 50% of women (Sharma et al., 1991; Alves et al., 2011).

A study found that the occurrence of signs and symptoms among women with trichomoniasis is higher than in those without the infection. The isolated use of symptomatology is still used to diagnose trichomoniasis, because in many public clinics there are no complementary diagnostic tests. Thus, a significant percentage of infected women are not diagnosed and treated (Alves et al., 2011).

This study verified that the prevalence of protozoan infection in the group of women with HIV was 3.9%. A similar prevalence was reported in another study, which found that trichomoniasis was present in 4.1% of HIV positive women, using culture as the diagnostic method (Silva et al., 2013). Several studies have shown that TV infection occurs more frequently in patients infected with HIV (Fastring et al., 2014; Van Der Pol et al., 2008; McClelland et al., 2007; Mason et al., 2005; Moodley et al., 2002). Some authors report that the rate of protozoan infection in these patients may range from 6% to 53% (Watts et al., 2005; Mcclelland et al., 2007; Fastring et al., 2014) and contribute to increased virus transmission. Those studies were carried out mostly with extremely poor socially and sexually vulnerable populations, with hardly any access to health services, such as those in African countries (Sorvillo et al., 2001; Moodley et al., 2002; McClelland et al., 2007).

The major drawbacks of our study were the limited sample size of HIV-positive women and the fact that those women have more frequent medical attention. This fact may help explain the absence of statistical association between HIV and TV infection, even in patients with AIDS. Similar results were observed in the USA when assessing the prevalence, incidence and recurrence of trichomoniasis among HIV positive and negative women. Furthermore, the rate of TV infection ranged from 9.4% to 29.5%. According to the authors, HIV infection did not increase TV prevalence and risk of recurrent or persistent trichomoniasis. Even with a prevalence higher than those observed in this study, the rate of TV infection did not vary due to the immune status or the $TCD4^{+}$ cell count, but due to other predisposing generally behavioral factors (Cu-Uvin et al., 2002).

Another study conducted in Brazil reported that TV infection was higher in the HIV-positive group, although this infection was not associated with the immune status of the patients but with behavioral factors, such as condom use, having a stable partner and medical follow-up (De Lemos & García-Zapata, 2014). Most of our patients (85.4%) were women with organic conditions similar to those of HIV-negative women, but differing from HIV-negative women in that those are patients who take better care of their health, presenting a low risk population, mainly for behavioral factors.

These data suggest that high rates of trichomoniasis among HIV-positive women, as seen in other studies, are associated with high-risk behavior. In this context, the use of drugs, smoking, presence of bacterial vaginosis, other STDs, black ethnicity and greater number of sexual partners are highlighted.

In the present study, we believe that the low prevalence of trichomoniasis in the HIV-infected group is due to the fact that screening and treatment can contribute to preventing transmission of sexually transmitted infections, even in asymptomatic patients (Cu-Uvin et al., 2002).

TV infection was present in 6.4% of the women studied, with evident lack of knowledge about this STI. Women who smoke are 3.57 times more likely to be infected. HIV status, TCD4 + cell count and viral load levels did not increase the risk of trichomoniasis. This fact can be due to adherence to the treatment and periodic consultations, which lead to the success of antiretroviral therapy and consequent control of opportunistic diseases, such as trichomoniasis.

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REFERENCES

1. Alves MJ, Oliveira R, Balteiro J, Cruz A. Epidemiologia de *Trichomonas vaginalis* em mulheres. *Rev Port Saúde Pública 29*: 27-34, 2011.
2. Barcelos MRB, Vargas PRM, Baroni C, Miranda AE. Infecções genitais em mulheres atendidas em Unidade Básica de Saúde: prevalência e fatores de risco. *Rev Bras Ginecol Obstet 30*: 349-354, 2008.
3. Brasil. Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente Transmissíveis (IST). In: *Brasília, DF: Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, Aids e Hepatites Virais*. 2015. 175p.
4. Bravo RS, Giraldo PC, Carvalho NS, Gabiatti JRE, Val ICC, Giraldo HPD, Passos MDL. Tricomoníase Vaginal: o que se Passa? *DST J Bras Doenças Sex Transm 22*: 73-80, 2010.
5. Chun, HM, Carpenter RJ, Macalino GE, Crum-Cianflone NF. The role of sexually transmitted infections in HIV-1 progression: A comprehensive review of the literature. *J Sex Trans Dis 2013:* 1-15, 2013.
6. Cu-Uvin S, Hyejin K, Jamieson DJ, Hogan JW, Schuman P, Anderson J, Robert SK. Prevalence, incidence, and persistence or recurrence of trichomoniasis among human immunodeficiency virus (HIV)-positive women and among HIV-negative women at high risk for HIV infection. *Clin Infect Dis 34*: 1406-1411, 2002.
7. De Lemos PAP, García-Zapata MTA. Aspects of *Trichomonas vaginalis*' infection and diagnostic methods. *Acta Obstet Ginecol Port 8*: 152-162, 2014.
8. Diamond LS. The establishment of various trichomonads of animals and man in axenic cultures. *J Parasitol 43*: 488-490, 1957.
9. Fastring DR, Amedee A, Gatski M, Clark RA, Mena LA, Levison J, Schmidt N, Rice J, Gustat J, Kissinger P. Co-occurrence of *Trichomonas vaginalis* and bacterial vaginosis and vaginal shedding of HIV-1 RNA. *Sex Transm Dis 41*: 173-179, 2014.
10. Furber AS, Maheswaran R, Newell J, Carroll C. Is smoking tobacco an independent risk factor for HIV infection and progression to AIDS? A systemic review. *Sex Transm Dis 83*: 41-46, 2007.
11. Grama DF, Casarotti LS, Morato MGVA, Silva LS, Mendonça DF, Limongi JE, Viana JC, Cury MC. Prevalence of *Trichomonas vaginalis* and risk factors in women treated at public health units in Brazil: a transversal study. *Trans R Soc Trop Med Hyg 107*: 584-591, 2013.
12. Grama DF, Casarotti LS, Limongi JE, Silva AL, Viana JC, Costa FC, Faria ESM, Cury MC. Inquérito preliminar de *Trichomonas vaginalis* em população feminina e fatores de risco associados em Unidade de Atendimento público no município de Uberlândia-MG. *Rev Patol Trop 39:* 91-104, 2010.
13. Klinger EV, Kapiga SH, Sam NE, Aboud S, Chen CY, Ballard RC, Larsen U. A community-based study of risk factors for *Trichomonas vaginalis* infection among women and their male partners in Moshi urban district, northern Tanzania. *Sex Transm Dis 33*: 712-718, 2006.
14. Landers DV, Wiesenfeld HC, Heine RP, Krohn MA, Hillier SL. Predictive value of the clinical diagnosis of lower genital tract infection in women. *Am J Obstet Gynecol 190*: 1004-1008, 2004.

15. Leon SR, Konda KA, Bernstein KT, Pajuelo JB, Rosasco AM, Caceres CF, Coates TJ, Klausner JD. *Trichomonas vaginalis* infection and associated risk factors in a socially-marginalized female population in coastal Peru. *Infect Dis Obstet Gynecol 2009*: 1-6, 2009.

16. Lewis DA. Trichomoniasis. *Medicine 38*: 291-293, 2010.

17. Mason PR, Fiori PL, Cappuccinelli P, Rappelli P, Gregson S. Seroepidemiology of *Trichomonas vaginalis* in rural women in Zimbabwe and patterns of association with HIV infection. *Epidemiol Infect 133*: 315-323, 2005.

18. McClelland RS, Sangaré L, Hassan WM, Lavreys L, Mandaliya K, Kiarie J, Ndinya-Achola J, Jaoko W, Baeten KM. Infection with *Trichomonas vaginalis* increases the risk of HIV-1 acquisition. *J Infect Dis 195*: 698-702, 2007.

19. Mirmonsef P, Krass L, Landay A, Spear GT. The role of bacterial vaginosis and trichomonas in HIV transmission across the female genital tract. *Curr HIV Res 10*: 202-210, 2012.

20. Moodley P, Wilkinson D, Connolly C, Moodley J, Sturm AW. *Trichomonas vaginalis* is associated with pelvic inflammatory disease in women infected with human immunodeficiency virus. *Clin Infect Dis 34*: 519-522, 2002.

21. Muzny CA, Rivers CA, Austin EL, Schwebke JR. *Trichomonas vaginalis* infection among women receiving gynaecological care at an Alabama HIV Clinic. *Sex Transm Infect 89*: 514-518, 2013.

22. Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, Stevens G, Gottlieb S, Kiarie J, Temmerman M. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. *PloS One 10:* e0143304, 2015.

23. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. *J Clin Microbiol 29*: 297-301, 1991.

24. Rughooputh S, Greenwell P. *Trichomonas vaginalis*: paradigm of a successful sexually transmitted organism. *Br J Biomed Sci 62*: 193-200, 2005.

25. Sharma P, Malla N, Gupta I, Ganguly N, Mahajan R. A comparison of wet mount, culture and enzyme linked immunosorbent assay for the diagnosis of trichomoniasis in women. *Trop Geogr Med 43*: 257-260, 1991.

26. Silva L, Miranda CFAE, Batalha RS, Monte RL, Talhari S. *Trichomonas vaginalis* and associated factors among women living with HIV/AIDS in Amazonas, Brazil. *Braz J Infect Dis 17*: 701-703, 2013.

27. Sorvillo F, Smith L, Kerndt P, Ash L. *Trichomonas vaginalis*, HIV, and African-Americans. *Emerg Infect Dis 7*: 927-932, 2001.

28. Swartzendruber A, Sales JM, Brown JL, DiClemente RJ, Rose ES. Correlates of incident *Trichomonas vaginalis* infections among African American female adolescents. *Sex Transm Infect 41*: 240-245, 2014.

29. Van Der Pol B, Kwok C, Pierre-Louis B, Rinaldi A, Salata RA, Chen PL, Van De Wijgert J, Mmiro F, Mugerwa R, Chipato T. *Trichomonas vaginalis* infection and human immunodeficiency virus acquisition in African women. *J Infect Dis 197:* 548-554, 2008.

30. Wang CC, McClelland RS, Reilly M, Overbaugh J, Emery RS, Mandaliya K, Chohan B, Ndinya-Achola J, Bwayo J, Kreiss JK. The effect of treatment of vaginal infections on shedding of human immunodeficiency virus type 1. *J Infect Dis 183:* 1017-1022, 2001.

31. Watts DH, Fazarri M, Minkoff H, Hillier SL, Sha B, Glesby M, Levine AM, Burk R, Palefsky JM, Moxley M. Effects of bacterial vaginosis and other genital infections on the natural history of human papillomavirus infection in HIV-1–infected and high-risk HIV-1–uninfected women. *J Infect Dis 191*: 1129-1139, 2005.