The Effect of Treatment of Vaginal Infections on Shedding of Human Immunodeficiency Virus Type 1

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To assess the effect of treatment of vaginal infections on vaginal shedding of cell-free human immunodeficiency virus type 1 (HIV-1) and HIV-1–infected cells, HIV-1–seropositive women were examined before and after treatment of Candida vulvovaginitis, Trichomonas vaginitis, and bacterial vaginosis. For Candida (n = 98), vaginal HIV-1 RNA decreased from 3.36 to 2.86 log$_{10}$ copies/swab (P < .001), as did the prevalence of HIV-1 DNA (36% to 17%; odds ratio [OR], 2.8; 95% confidence interval [CI], 1.3–6.5). For Trichomonas vaginitis (n = 55), HIV-1 RNA decreased from 3.67 to 3.05 log$_{10}$ copies/swab (P < .001), but the prevalence of HIV-1 DNA remained unchanged (22%–25%; OR, 0.8; 95% CI, 0.3–2.2). For bacterial vaginosis (n = 73), neither the shedding of HIV-1 RNA (from 3.11 to 2.90 log$_{10}$ copies/swab; P = .14) nor the prevalence of DNA (from 21% to 23%; OR, 0.8; 95% CI, 0.3–2.0) changed. Vaginal HIV-1 decreased 3.2- and 4.2-fold after treating Candida and Trichomonas, respectively. These data suggest that HIV-1 transmission intervention strategies that incorporate diagnosis and treatment of these prevalent infections warrant evaluation.

Important contributions to the understanding of the association between sexually transmitted diseases (STDs) and the transmission of human immunodeficiency virus type 1 (HIV-1) have been made in the past decade. STDs may serve as a cofactor for transmission of HIV-1 by increasing both susceptibility of an uninfected partner (in the case of sexual transmission) and infectivity of an infected individual (in the case of sexual and vertical transmission) [1].

For HIV-1–infected women with STDs, it has been hypothesized that increased shedding of HIV-1 in the presence of cervical or vaginal infections may increase infectivity [1]. Vertical transmission studies provide the best available evidence that shedding of HIV-1 in the female genital tract is associated with increased transmission risk. Several studies have demonstrated that the detection of HIV-1 in the birth canal is associated with infant infection [2–4].

Studies in women have established that genital ulcer disease [5–6] and cervical infections [5, 7–10] are risk factors for the detection of genital HIV by nucleic acid–based assays. Furthermore, 4 studies have examined the association between vaginal infections and vaginal shedding of HIV-1 DNA or RNA [5, 7, 8, 10]. In a study of 318 HIV-1–seropositive women in Mombasa, Kenya, Mostad et al. [10] evaluated shedding of HIV-1–infected cells, as measured by HIV-1 DNA assay. Vaginal yeast infection was associated with a 2-fold increased likelihood of detection of HIV-1–infected cells on vaginal swabs. In contrast, Trichomonas vaginitis and bacterial vaginosis were not associated with increased prevalence of shedding.

Four prospective studies in men and women have examined the effect of treatment of STDs on shedding of HIV-1 DNA or RNA [5, 11–13]. Three studies in men have reported that treatment of gonococcal urethritis resulted in a decrease in shedding of cell-free HIV-1 or infected cells [11–13]. Data from a prospective study in women found that treatment of gonorrhea resulted in a significant decrease in the prevalence of shedding of cell-free HIV-1 [5]. Treatment of chlamydial cervicitis and cervicovaginal ulcer also was associated with a decrease in shedding of cell-free HIV-1, although the association was not statistically significant. Trichomonas vaginitis, Candida vulvo-vaginitis, and bacterial vaginosis were not evaluated.

To further explore the relationship between vaginal infections and vaginal shedding of both cell-free HIV-1 and HIV-1–infected cells, we conducted a prospective study in which samples were...
obtained from women before and after treatment of Candida vulvovaginitis, Trichomonas vaginitis, and bacterial vaginosis.

Methods

Study population and procedures. Between August 1996 and September 1998, women attending the STD and family planning clinics at Coast Provincial General Hospital were referred to a research clinic if they desired HIV testing. Women were tested for HIV-1 antibodies, using a rapid-detection assay. Women who tested positive and complained of genital tract symptoms were recruited into the study.

At enrollment, a questionnaire was administered concerning demographic, sexual, contraceptive, and obstetric history and current symptoms. A physical examination was done, including a detailed genital tract examination. Vaginal samples for HIV-1 DNA and RNA analysis were obtained by placing a Dacron swab firmly on the vaginal wall and rolling 3 times between the fingertips. Vaginal secretions were collected for Gram’s staining, to assess inflammation and diagnosis of bacterial vaginosis, for wet-mount analysis for Candida and Trichomonas vaginalis, for culture for T. vaginalis and lactobacillus, and for pH measurement (ColorpHast 4.0–7.0; EM Reagents). Cervical secretions then were collected for Gram’s stain diagnosis of cervicitis, for Neisseria gonorrhoeae culture, and for a Chlamydia trachomatis antigen test. Examinations and sample collections were done by 1 of 2 investigators (R.S.M. or C.C.W.).

Women received treatment for vaginal infections either on the day of examination or 2 days later, during a follow-up visit, when laboratory results were available. Patients with Candida vulvovaginitis were treated with nystatin vaginal suppositories twice a day for 14 days. Patients with Trichomonas vaginalis or bacterial vaginosis were treated with metronidazole (400 mg) twice a day for 10 days. Women were asked to return in 2 weeks for a repeat examination, including collection of swab samples for HIV-1 DNA and RNA analysis. If Candida vulvovaginitis had not resolved by the follow-up examination, the patient was treated with fluconazole (100 mg orally) twice a day for 3 days. If Trichomonas vaginalis or bacterial vaginosis persisted at follow-up examination, patients were treated again, using the same regimen.

Initial and follow-up visits for each woman were paired according to substudy. Women were designated to be in the Candida vulvovaginitis, Trichomonas vaginitis, or bacterial vaginosis substudies on the basis of results of their initial laboratory tests. Women were included in a substudy analysis only if they had no other diagnosed vaginal or cervical infection, with one exception. Because of the high background prevalence of bacterial vaginosis in this population, women with concurrent bacterial vaginosis were included in the Candida vulvovaginitis and Trichomonas vaginitis substudies. A woman could be enrolled in ≥1 substudy if she developed a subsequent vaginal infection with a different organism.

Follow-up visits were included in the analysis if they occurred ≥13 days after and within 90 days of the initial visit and if the diagnosis of interest had resolved. Sixty-one follow-up visits did not meet these criteria. If bacterial vaginosis was present at the follow-up examination for Candida or Trichomonas vulvovaginitis, the visit was still included. Women using hormonal contraception or intrauterine devices were included in the analysis if their contraceptive method did not change between initial and follow-up visits. Women with genital ulcer disease or cervical infection at either visit were excluded.

Laboratory tests. Gram’s-stained vaginal and cervical samples were examined for the presence of inflammation, as indicated by the number of polymorphonuclear leukocytes in 3 nonadjacent, high-power fields. Bacterial vaginosis was diagnosed by using a 10-point system based on the presence of lactobacilli and Gardnerella, Bacteroides, and Mobiluncus species morphotypes [14]. Lactobacillus species were cultured on Ragosa agar (Difco). T. vaginalis was cultured in Diamonds modified media (JRH Biosciences), and N. gonorrhoeae was cultured on modified Thayer-Martin media. C. trachomatis antigen was detected by use of an EIA (Syva). The presence of spermatozoa was noted on wet mount and on Gram’s-stained vaginal and cervical samples.

The diagnosis of Candida vulvovaginitis was established if the wet mount or vaginal Gram’s stain (or both) were positive for budding yeast or hyphae. The diagnosis of Trichomonas vaginitis was made by wet mount or Trichomonas culture (or both). Bacterial vaginosis was diagnosed by using a 10-point scale, with scores of 7–10 being diagnostic of bacterial vaginosis [14].

HIV-1 antibody testing was done with a rapid-detection assay (Capillus HIV-1/HIV-2; Cambridge Biotech). Positive tests were confirmed by EIA (Recombigen; Cambridge Biotech). CD4 lymphocyte concentration was measured by a manual (Coulter) or an automated (Zymmunne) method.

Vaginal swabs for HIV-1 DNA detection were stored in dry cryovials at −70°C in Mombasa, were shipped to the Fred Hutchinson Cancer Research Center (Seattle) on dry ice, and were stored again at −70°C. The presence of HIV-1–infected cells or proviral DNA was measured on a sample volume of 2 μL, using a qualitative assay. Nested polymerase chain reaction amplification of the gag gene was used to detect the presence of HIV-1 DNA, as described elsewhere [8, 13], with a lower limit of detection of 1 copy. For the current study, the protocol was changed slightly to reduce inhibition (the concentration of MgCl2 was changed to 2.5 mM, and bovine serum albumin was added).

Vaginal swabs for HIV-1 RNA detection were placed in cryovials containing 1 mL of liquid freezing medium (70% RPMI, 20% fetal calf serum, and 10% DMSO, with added penicillin, streptomycin, and amphotericin B), were placed immediately on ice, and were transferred within 90 min into a container that permitted gradual cooling of the vial to −70°C. Samples were stored and were shipped in liquid nitrogen. A quantitative HIV-1 assay (Gen-Probe) was used to measure virus levels on a sample volume of 200 μL. This assay has been shown to quantitatively detect the subtypes of HIV-1 present in Kenya [15] and has been demonstrated to quantitatively detect HIV-1 RNA on swab samples in experiments in which known quantities of cell-free HIV-1 were spiked onto Dacron swabs. Assay measurements of swab and plasma HIV-1 concentration agreed within 3-fold (D. D. P. Panteleef, Fred Hutchinson Cancer Research Center, personal communication).

In previous studies of HIV-1 RNA in plasma samples, we assigned a lower limit of quantitation of 25 copies per assay. For plasma, this translated to a limit of 30 copies/mL, because 500 μL was tested in each assay [16]. In this study, we also considered 25 copies per assay as the limit at which the data were quantitative.
Thus, in the cases in which we tested 200 µL from a swab lysed in 1 mL of buffer, the lower limit of quantitation was calculated to be 125 copies per swab.

Data were considered valid if results from duplicate assays of 200-µL aliquots of the swab sample agreed within 3-fold of each other. If results of the duplicate assays did not agree within 3-fold, a repeat run with duplicate assays was done. This procedure was followed unless both results were less than the level of quantitation, in which case the assay result was assigned to half the lower limit, or 12.5 copies (this occurred 27 of 442 times). Results from the second run were used if the results were within 3-fold agreement or if the duplicate assays were both <25 copies per assay. If not, the results were considered invalid, and the sample was excluded from the analysis of RNA results. Ten samples were excluded on this basis. For valid assays, the average of the duplicate assay results was used in the data set.

Data analysis. Statistical analyses were performed using SPSS (version 8.0; SPSS) and Stata (version 4.0; Stat). Paired Student’s t tests were used to compare average HIV-1 RNA log_{10} copies per swab before and after treatment of vaginal infections. Within each substudy, paired Student’s t tests were used to compare the reduction in shedding between women with and without symptoms, signs, and laboratory evidence of severity of vaginal infection.

McNemar’s test for paired data was used to estimate the association between the detection of HIV-1 DNA and vaginal infection and the correlation between RNA and DNA results.

Analyses of the Candida and Trichomonas vaginitis substudies were done with and without adjusting for the concurrent diagnosis of bacterial vaginosis. In addition, the presence of spermatozoa may indicate HIV DNA or RNA introduced by the male partner and therefore was considered in the analysis. Generalized estimating equations were used to examine these potential confounders.

Results

Patient characteristics. Two hundred three women were included in the study, including 31 who participated in 2 substudies and 4 who participated in 3 substudies. Thus, 242 episodes of vaginal infection are included. Enrollment characteristics of the study subjects are listed in table 1. The median age was 25 years, and only 17% of women had studied beyond primary school. Most women described themselves as married, monogamous, and/or abstinent. Although 48% described symptoms consistent with HIV-1 disease, only 27% had a CD4 cell count <200 cells/µL. The microbiologic characteristics of the vaginal infections are presented in table 2. The median time between paired sample collections was 20 days (range, 13–90 days).

Candida vulvovaginitis. Ninety-eight women with Candida vulvovaginitis were included in the analysis. Two women had missing swabs, and 3 had invalid RNA results. Among the remaining 93 women, the mean concentration of HIV-1 RNA in vaginal fluids decreased 3.2-fold after treatment, from a mean of 3.36 to 2.86 log_{10} copies/swab (P < .001; table 3). In a similar manner, the prevalence of HIV-1 DNA in 98 women decreased significantly after treatment, from 36% to 17% (odds ratio [OR], 2.8; 95% confidence interval [CI], 1.3–6.5; P = .005). Adjusting for the presence of bacterial vaginosis or spermatozoa did not materially alter the results.

To investigate whether the effect of treatment on shedding of HIV-1 was more pronounced among women with more severe vaginal infection, we compared the reduction in shedding in women with and without symptoms, signs, and laboratory evidence of vulvovaginitis (table 4). Vulvar erythema on initial examination was associated with a significantly greater reduction in genital HIV-1 RNA after treatment (P = .02), but there was no significant effect of vulvar itching, vaginal discharge, laboratory evidence of inflammation, or hyphal fungal elements on vaginal gram stain.

Trichomomas vaginitis. Among 67 women with Trichomonas vaginitis, 55 had valid RNA results (6 women had missing swab samples, and 6 had invalid RNA results). Treatment of infection in these women resulted in a 4.2-fold reduction in mean HIV-1 copies per swab (3.67 to 3.05 log_{10} copies/swab; P < .001; table 3). However, among 67 women with DNA results, there was no significant change in the prevalence of DNA shedding before and after treatment (from 22% to 25%; OR, 0.8; 95% CI, 0.3–2.2). Results were not affected by statistical adjustment for the presence of bacterial vaginosis or spermatozoa.

The reduction in log_{10} HIV-1 RNA concentration was significantly greater in women with inflammation, as determined by Gram’s stain at the time of infection than among women without inflammation (table 4). Results did not differ on the basis of the presence or absence of itching or signs of vaginal discharge.

Bacterial vaginosis. Among 77 women with bacterial vaginosis, there was no significant reduction in either RNA levels or DNA shedding (table 3). Three women had missing swab samples, and 1 had invalid RNA results. The mean vaginal

| Table 1. Enrollment characteristics for 199 (unless otherwise stated) human immunodeficiency virus type 1 (HIV)-seropositive women in Mombasa, Kenya. |
|---------------------------------|---|
| Characteristic | No. (%) |
| Marital status | | |
| Never married | 25 (13) |
| Married | 138 (69) |
| Separated or widowed | 36 (18) |
| More than primary school education | 34 (17) |
| Contraceptive use during last intercourse | | |
| None | 185 (93) |
| Condom | 2 (1) |
| Oral contraceptive | 1 (5) |
| Depo medroxyprogesterone acetate | 5 (2.5) |
| Intrauterine device | 1 (5) |
| Tubal ligation | 5 (2.5) |
| Monogamous or abstinent in the past year | 162 (81) |
| Money for sex in past year | 2 (1) |
| Pregnant | 9 (4.5) |
| Symptoms consistent with HIV infection^b | 97 (49) |
| CD4 cell count <200 cells/µL (n = 183) | 50 (27) |

NOTE. Median age of the women was 25 years (range, 16–49 years).

^a Data on 4 patients are missing.

^b Cough or diarrhea for >1 month, weight loss of >4.5 kg, or shingles in past 2 years.
Trichomonas substudy ($n$)

Bacterial vaginosis substudy ($n$)

shedding patterns of cell-free HIV-1 and HIV-1-infected cells may reflect distinct characteristics of these vaginal pathogens and the host immune response within the vaginal compartment.

Local recruitment of CD4 receptor–bearing lymphocytes in the vaginal mucosa has been reported in Candida vulvovaginitis [17, 18], whereas Trichomonas infection has been shown to elicit a predominantly polymorphonuclear phagocytic response [19]. In contrast, bacterial vaginosis is characterized by the absence of inflammatory cells [20]. Thus, the decrease in shedding of HIV-1–infected cells after treatment of Candida vulvovaginitis may reflect resolution of an organism-specific host immune response.

On the other hand, shedding of cell-free HIV-1 may be related to factors that affect HIV-1 replication rates in infected cells. HIV-1 replicates at higher levels in activated T cells than in resting cells [21]. Thus, the decrease in shedding of cell-free virus after treatment of Candida vulvovaginitis or Trichomonas vaginitis may reflect a reduction in the level of local T cell activation once infection has resolved.

An alternate mechanism also may be proposed. Vulvar and vaginal erythema are characteristic of both Candida vulvovaginitis and Trichomonas vaginitis [22]. The associated subepithelial blood vessel dilation [23] may result in increased delivery of cell-free virus to the vagina; subsequent disruption of intercellular junctions and increased extravasation of vaginal fluid [24] may result in increased movement of cell-free HIV-1 into the vaginal lumen. In this study, the observation of a more pronounced reduction in shedding in women with evidence of severe vulvar or vaginal inflammation at the time of infection suggests an association between mucosal inflammation and shedding of cell-free HIV-1.

No studies have directly examined the role of vaginal STDs on female-to-male transmission of HIV-1. The relevance of our results depends on the degree to which shedding of cell-free HIV-1 or HIV-1–infected cells reflects infectivity. Studies that report an association between detection of HIV-1 DNA or RNA in the maternal genital tract and infant infection provide epidemiologic evidence for an association between shedding of HIV-1 genetic material and infectivity [2–4]. Another study suggested that female genital tract shedding of infected cells, as measured by proviral DNA, was associated with sexual transmission of in-

**Table 2.** Laboratory characteristics of Candida vaginitis, Trichomonas vaginitis, and bacterial vaginosis in women infected with human immunodeficiency virus type 1.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Enrollment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Candida substudy ($n = 98$)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram’s stain positive for Candida</td>
<td>91</td>
<td>0</td>
</tr>
<tr>
<td>Wet mount positive for Candida</td>
<td>83</td>
<td>0</td>
</tr>
<tr>
<td>Vaginal PMNL count, median (range), cells/hpf</td>
<td>4 (0–55)</td>
<td>1 (0–61)</td>
</tr>
<tr>
<td>pH, median (range)</td>
<td>5.0 (4–7)</td>
<td>5.0 (4–7)</td>
</tr>
<tr>
<td>Sperm</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Concurrent bacterial vaginosis</td>
<td>29</td>
<td>20</td>
</tr>
<tr>
<td><strong>Trichomonas substudy ($n = 67$)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wet mount positive for Trichomonas</td>
<td>96</td>
<td>0</td>
</tr>
<tr>
<td>Culture positive for Trichomonas</td>
<td>91</td>
<td>0</td>
</tr>
<tr>
<td>Vaginal PMNL count, median (range), cells/hpf</td>
<td>9 (0–78)</td>
<td>2 (0–34)</td>
</tr>
<tr>
<td>pH (median, range)</td>
<td>7.0 (4–7)</td>
<td>5.3 (4–7)</td>
</tr>
<tr>
<td>Sperm</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Concurrent bacterial vaginosis</td>
<td>54</td>
<td>33</td>
</tr>
<tr>
<td><strong>Bacterial vaginosus substudy ($n = 77$)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clue cells positive</td>
<td>82</td>
<td>8</td>
</tr>
<tr>
<td>Lactobacillus culture negative</td>
<td>83</td>
<td>76</td>
</tr>
<tr>
<td>Score, median (range)</td>
<td>8 (7–10)</td>
<td>3 (0–6)</td>
</tr>
<tr>
<td>Vaginal PMNL count, median (range), cells/hpf</td>
<td>2 (0–39)</td>
<td>2 (0–68)</td>
</tr>
<tr>
<td>pH, median (range)</td>
<td>5.8 (4–7)</td>
<td>5.0 (4–7)</td>
</tr>
<tr>
<td>Sperm</td>
<td>16</td>
<td>13</td>
</tr>
</tbody>
</table>

NOTE. Data are percentages unless otherwise indicated. hpf, high-power field; PMNL, polymorphonuclear leukocytes.

HIV-1 RNA level in 73 women with valid results was $3.11 \log_{10}$ copies/swab before treatment and $2.90 \log_{10}$ copies/swab after treatment ($P = .14$). Prevalence of HIV-1 DNA was 21% before treatment and 23% after treatment (OR, 0.8; 95% CI, 0.3–2.0). Severity of bacterial vaginosis did not significantly alter the change in HIV-1 RNA before and after treatment (table 4).

**Correlation between HIV-1 RNA and DNA.** Detection of vaginal HIV-1 DNA and quantitative detection of HIV-1 RNA were highly correlated ($P < .01$). HIV-1 RNA was detected in 75% of samples and HIV-1 DNA in 26% of samples. It is difficult to directly compare the prevalence of RNA and DNA because there are differences in both the amount of sample analyzed and in the type of assays used.

**Discussion**

In this prospective study, treatment of Candida vulvovaginitis resulted in a 3.2-fold reduction in the concentration of cell-free virus in vaginal secretions and in an $\approx 3$-fold decrease in the likelihood of detecting HIV-1–infected cells (OR, 2.8; 95% CI, 1.3–6.5). Treatment of Trichomonas vaginitis resulted in a 4.2-fold reduction in the quantity of cell-free virus in vaginal secretions but did not result in a decrease in shedding of HIV-1–infected cells. In contrast, treatment of bacterial vaginosis did not result in a reduction of either cell-free HIV-1 or HIV-1–infected cells. For Candida vulvovaginitis, Trichomonas vaginitis, and bacterial vaginosis, the differential effect of treatment on vaginal shedding patterns of cell-free HIV-1 and HIV-1–infected cells may reflect distinct characteristics of these vaginal pathogens and the host immune response within the vaginal compartment.

**Table 3.** Vaginal shedding of human immunodeficiency virus type 1 (HIV-1) RNA and DNA before and after treatment of vaginitis in HIV-1–infected women.

<table>
<thead>
<tr>
<th>HIV-1 RNA or DNA shedding</th>
<th>Before resolution</th>
<th>After resolution</th>
<th>OR (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RNA, mean log$_{10}$ copies/swab</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida vulvovaginitis ($n = 93$)</td>
<td>3.36</td>
<td>2.86</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Trichomonas ($n = 55$)</td>
<td>3.67</td>
<td>3.05</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Bacterial vaginosis ($n = 73$)</td>
<td>3.11</td>
<td>2.90</td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td><strong>DNA, prevalence, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida vulvovaginitis ($n = 98$)</td>
<td>36</td>
<td>17</td>
<td>2.8 (1.3–6.5)</td>
<td>.005</td>
</tr>
<tr>
<td>Trichomonas ($n = 67$)</td>
<td>22</td>
<td>25</td>
<td>0.8 (0.3–2.2)</td>
<td>.8</td>
</tr>
<tr>
<td>Bacterial vaginosis ($n = 77$)</td>
<td>21</td>
<td>23</td>
<td>0.8 (0.3–2.0)</td>
<td>.8</td>
</tr>
</tbody>
</table>

NOTE. CI, confidence interval; OR, odds ratio.
tion [25]. Our results, combined with considerable evidence for the importance of genital infections in potentiating HIV-1 transmission, suggest that treatment of *Candida* vulvovaginitis and *Trichomonas* vaginitis may reduce the infectivity of women with HIV-1 infection. Although there is evidence that bacterial vaginosis may be a risk factor for acquisition of HIV-1 infection [26–27], our data do not support increased infectivity of HIV-1–seropositive women with this condition.

Both *Candida* vulvovaginitis and *Trichomonas* vaginitis are common conditions. In cross-sectional surveys of family planning or of prostitute populations in Africa, point prevalence of *Candida* vulvovaginitis has ranged from 10% to 13% [28–30], and the prevalence of *Trichomonas* vaginitis in women at an STD clinic in Kenya has been reported as 23% [31]. Among HIV-1–seropositive women, the prevalence of *Candida* vulvovaginitis has been reported to be as high as 62% [32]. In contrast, the prevalence of genital ulcer disease has ranged from <1% to 5% [29–30], and the prevalence of cervicitis in the same populations has ranged from 3% to 7% [28, 29]. Despite the high prevalence of both *Candida* vulvovaginitis and *Trichomonas* vaginitis, most studies reporting an association between STDs and HIV infection have focused on the role of genital ulcer disease and cervical infections.

In this prospective study, we report that treatment of *Candida* vulvovaginitis may result in a 3.2-fold decrease in the quantity of cell-free HIV-1 and an ~3-fold decrease in the likelihood of detecting HIV-1–infected cells in the vaginal fluid of HIV-1–seropositive women. Treatment of *Trichomonas* vaginitis resulted in a 4.2-fold reduction in the quantity of cell-free HIV-1 but did not affect the prevalence of HIV-1–infected cells. Given the high prevalence of *Candida* vulvovaginitis and *Trichomonas* vaginitis among HIV–1–infected women, even a modest association with potential infectivity may lead to a substantial attributable risk for HIV-1 transmission. Efforts to reduce the incidence and duration of *Candida* vulvovaginitis and *Trichomonas* vaginitis may substantially reduce the infectivity of HIV-1–infected women and could have a measurable impact on the HIV-1 epidemic.

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### References


### Table 4: Stratified analysis of shedding of human immunodeficiency virus type 1 (HIV-1) RNA in women before and after treatment of vaginal infections.

<table>
<thead>
<tr>
<th>Vaginal infection</th>
<th>Variable present</th>
<th>Variable absent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean reduction, log$_\text{10}$ HIV-1 RNA copies/swab</td>
</tr>
<tr>
<td><em>Candida</em> vulvovaginitis ($n = 93$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvar itching</td>
<td>49</td>
<td>0.43</td>
</tr>
<tr>
<td>Abnormal vaginal discharge</td>
<td>53</td>
<td>0.68</td>
</tr>
<tr>
<td>Vulvar erythema</td>
<td>18</td>
<td>1.05</td>
</tr>
<tr>
<td>Vaginal PMNL count $\geq$10</td>
<td>19</td>
<td>0.50</td>
</tr>
<tr>
<td>Presence of hyphae on Gram’s stain</td>
<td>59</td>
<td>0.57</td>
</tr>
<tr>
<td><em>Trichomonas</em> vaginitis ($n = 55$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvar itching</td>
<td>17</td>
<td>0.53</td>
</tr>
<tr>
<td>Abnormal vaginal discharge</td>
<td>23</td>
<td>0.59</td>
</tr>
<tr>
<td>Vaginal PMNL count $\geq$10</td>
<td>26</td>
<td>1.00</td>
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<tr>
<td>Bacterial vaginosis ($n = 73$)</td>
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</tr>
<tr>
<td>Complaint of vaginal discharge</td>
<td>23</td>
<td>0.52</td>
</tr>
<tr>
<td>Abnormal vaginal discharge</td>
<td>32</td>
<td>0.36</td>
</tr>
<tr>
<td>Nugent score $\geq$9</td>
<td>16</td>
<td>(0.02)$^a$</td>
</tr>
</tbody>
</table>

*NOTE:* PMNL, polymorphonuclear leukocytes.

$^a$ Log$_{10}$ HIV-1 RNA copies/swab increased by 0.02 after treatment.
17. Fouts AC, Kraus SJ. Trichomonas vaginalis: reevaluation of its clinical pre-