SPECIAL SECTION: HIV/AIDS

Gynecologic Infections in Human Immunodeficiency Virus–Infected Women

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The maturation of the acquired immunodeficiency syndrome epidemic has now claimed more than 12 million women worldwide, the majority in undeveloped countries where human immunodeficiency virus (HIV) and sexually transmitted infections coexist and interact synergistically. Among HIV-infected women, there is excessive morbidity due to sexually transmitted diseases (STDs) and gynecologic disorders. This review summarizes the expanding understanding of vaginal flora, vaginitis, cervicitis, pelvic inflammatory disease, and genital ulcer disease in HIV-infected women. In addition to the altered clinical course, complications, and management difficulties of STDs, some gynecologic infections may influence HIV transmission as well as the vertical transmission of HIV to the newborn. Finally, severe immunodeficiency allows unusual opportunistic pathogens to invade the upper and lower genital tract. Control and prevention of gynecologic infections in HIV-positive and HIV-negative women are key components to preventing further HIV transmission.

Since HIV is frequently sexually transmitted, it follows that women who are HIV-seropositive are likely to acquire other sexually transmitted infections and diseases (STDs). The presence of an STD appears to increase the risk of both acquiring and transmitting HIV [1, 2]. In the presence of HIV infection, particularly with the immunodeficiency of AIDS, the clinical presentation, course, complications, and response to conventional therapy of these STDs, as well as noninfectious gynecologic disease, may be modified. Moreover, the clinical course of HIV disease may sometimes be altered by coexistent STDs. Finally, many gynecologic infections may affect HIV bidirectional transmission [3]. Hence, successful management of gynecologic infections in any given woman not only benefits the individual patient but has the potential to reduce HIV transmission to uninfected males or to reduce the woman’s risk of becoming infected with HIV [4]. Both the biological consequences of HIV infection and the behaviors of populations at risk of HIV infection might be expected to predispose women to gynecologic infectious complications [1, 2] (table 1).

Among HIV-infected women, there is excessive morbidity due to STDs and gynecologic disorders [5–9]. The need to prevent and control manifestations applies worldwide, but it is in the nonindustrialized world that gynecologic infections in HIV infection have their greatest impact, not only influencing HIV transmission but adding the dimension of vertical transmission of HIV to newborns [10]. The effect of coinfection with STDs and of STD treatment on HIV shedding in genital tract secretions was recently reviewed, but the authors arrived at few definitive conclusions and found little conclusive data on genital tract HIV shedding in women [11]. Although HIV load is substantially increased among men with urethritis, only 1 controlled prospective study showed a major reduction in HIV load after successful STD treatment in men [12]; data concerning women are lacking.

In the mid-1980s, women accounted for only 8% of all AIDS cases reported in the United States, but by the late 1990s the percentage had jumped to nearly 25%. Twelve million women worldwide are infected with HIV-1 [13], representing ~40% of infected individuals. The purpose of this review is to describe the epidemiology, clinical manifestations, and treatment of gynecologic infections in HIV-infected women.

Vaginal Flora in HIV-Seropositive Women

Recently, attention has been directed toward the protective role provided by normal Lactobacillus-dominant flora [14] in preventing STDs. There is evidence that women lacking lactobacilli are at higher risk of acquiring STDs, including HIV [15, 16]. The least-protective flora appears to lack lactobacilli of any species or function, whereas the most protective correlates with high numbers of H2O2-producing lactobacilli, which are also capable of elaborating lactic acid and other bacteriocins [16]. Several studies have observed substantial perturbations of vaginal flora in HIV-seropositive women; <20% have Lacto-
**Table 1. Interaction between human immunodeficiency virus infection and gynecologic infections.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bacterial vaginosis</th>
<th>Trichomoniasis</th>
<th>Candidiasis</th>
<th>Cervicitis</th>
<th>Cervical dysplasia (HPV)</th>
<th>Pelvic inflammatory disease</th>
<th>Genital herpes</th>
<th>Syphilis</th>
<th>Vulvar warts (HPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+ to ++</td>
<td>+</td>
<td>+</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>More common than in those without HIV</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
</tr>
<tr>
<td>More severe than in those without HIV</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes, ++</td>
<td>Perhaps</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Response to anti-infective therapy</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal (recurrent)</td>
<td>Unknown (high recurrence)</td>
<td>Unknown</td>
<td>Low recurrence</td>
<td>Diminished</td>
</tr>
<tr>
<td>Effect of gynecologic infection</td>
<td>Facilitates HIV transmission</td>
<td>Perhaps</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Increases cervicovaginal HIV-RNA load*</td>
<td>Perhaps</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
<td>--</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Yes</td>
<td>Perhaps</td>
</tr>
</tbody>
</table>

**NOTE.** Table is adapted from [96]. HPV, human papilloma virus; +, least; ++, most.

* Compared to controls with matched risk factors.
bacillus-dominant flora [16–18]. These epidemiological studies have also found high rates of so-called abnormal flora in behavior-matched HIV-seronegative control subjects, indicating that variations in vaginal flora are extremely common and are behavior-determined. These facts should not reduce the importance of protective flora in preventing gynecologic complications in all populations. Clearly, additional data are needed, as is demonstration that correction of abnormal flora can prevent local gynecologic disease and HIV transmission [16].

**Bacterial Vaginosis**

Bacterial vaginosis (BV) is recognized as the most common cause of vaginitis in the United States and has been reported to occur in 20%–50% of women in sub-Saharan Africa [19]. Previously considered to be only a nuisance because of the malodorous discharge it causes, BV now has been associated with preterm labor, premature rupture of membranes, chorioamnionitis, and disease of the upper genital tract.

Cohen et al. [20], in a cross-sectional study of female commercial sex workers in Chiang Mai, first reported a significant association between abnormalities of vaginal flora, clinically diagnosed BV, and HIV seropositivity. This association in multiple logistic regression analysis was independent of age, condom use, contraceptive method, and number of sexual contacts per week. It was suggested that BV increased the susceptibility of women to heterosexual transmission of HIV. Alternatively, the absence of lactobacilli that typifies BV might explain the vulnerability; that is, BV may be either a marker or a cofactor of HIV transmission. No evidence was presented that HIV infection predisposed to BV, although there was some evidence that the prevalence of BV increases with the degree of immunodeficiency.

Several additional cross-sectional and population-based studies have confirmed the association between BV and HIV seropositivity [21, 22]. Sewankambo et al. [21], who studied 4718 women in rural Uganda, observed that the increased frequency of HIV seropositivity was independent of age, condom use, contraceptive method, and number of sexual contacts per week. It was suggested that BV increased the susceptibility of women to heterosexual transmission of HIV. Alternatively, the absence of lactobacilli that typifies BV might explain the vulnerability; that is, BV may be either a marker or a cofactor of HIV transmission. No evidence was presented that HIV infection predisposed to BV, although there was some evidence that the prevalence of BV increases with the degree of immunodeficiency.

治疗BV的治疗包括保持阴道微生态平衡，促进阴道乳杆菌的生长，以及控制其他性传播疾病。BV的治疗需针对具体病原体进行，如乳杆菌的缺乏需要使用乳杆菌制剂，其他病原体则需针对具体病原体进行治疗。

**Trichomoniasis**

Caused by *Trichomonas vaginalis*, vaginal trichomoniasis is one of the most common STDs. It is estimated that 180 million persons worldwide are infected each year, including 3 million in the United States. Prevalence rates depend upon the population studied. In a study of pregnant women in the United States by Cotch et al. [26], trichomoniasis was observed in 12.6% of 13,816 women. Higher prevalence rates have been reported in the United States in STD clinics (38%) and among prison inmates (46.9%) [27, 28]. Even higher rates have been reported in underdeveloped countries [29, 30]. No correlation has been seen between degree of immunodeficiency, as measured by CD4 cell counts, and prevalence of trichomoniasis.

Trichomoniasis serves as a marker of high-risk sexual behavior [26] and is associated with both recognized and unrecognized HIV infection [31]. Both asymptomatic and symptomatic trichomoniasis are extremely common in HIV-infected women (RR, 2.0; 95% CI, 1.1–3.6) [29]. There is no evidence that the clinical spectrum of *Trichomonas vaginalis* is different in HIV-seropositive women, and there is no alteration in their response to metronidazole therapy, including relapse rates or incidence of metronidazole resistance. Nicolai et al. [32] recently reported a high rate of reinfection with *T. vaginalis* among HIV-infected women (36% within 8 years of the study period) and noted that a history of another STD predicted the likelihood of recurrence.

Similarly, the effect of severe immunodeficiency on trichomoniasis is unknown. Several authors, however, have emphasized the importance of vaginal trichomoniasis in increasing the bidirectional risk of HIV transmission [28–30, 33, 34]. Trichomoniasis may be responsible for a greater population-attributable risk of HIV-1 infection than genital ulcer disease because of its high prevalence in most populations. Trichomoniasis results in aggressive local cellular immune response, with heavy
infiltration of polymorphonuclear leukocytes even in asymptomatic patients. About 50% have punctate hemorrhages, which resulted in increased HIV access to the bloodstream and target cells as well as enhanced HIV shedding. This potentially amplifying influence on HIV transmission has led to the determination that T. vaginalis is one of the primary targets of mass population and syndromic STD treatment. Also of importance to HIV-seropositive pregnant women is the independent effect of trichomoniasis in contributing to adverse birth outcome, specifically premature rupture of membranes, preterm delivery, and low birth weight [26].

**Vulvovaginal Candidiasis**

Vulvovaginal candidiasis (VVC) differs substantially from other lower-genital-tract infections that are sexually transmitted. VVC, although associated with sexual activity, occurs extremely commonly in all strata of society—including celibate, premenopausal, and postmenopausal women—and is known to recur frequently in immunocompetent women. Moreover, Candida microorganisms are frequently found colonizing the vaginas of asymptomatic healthy women. The most important distinction in the United States is that most vaginal yeast infections today are self-diagnosed, often incorrectly, and usually self-treated.

In the late 1980s, 3 reports suggested that VVC was a unique problem in women infected with HIV [35–37]. The authors reported frequent, more prevalent, and recurrent VVC in HIV-infected women, which tended to be refractory to antifungal therapy. Rhoads et al. [35] concluded that recurrent VVC was an indicator of not only HIV infection but also severe underlying immunodeficiency and was associated with a poor prognosis. Unfortunately, the earlier studies lacked control groups, especially those matched for sexual behavior, antibiotic exposure, etc. Nevertheless, in response, the Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration took rapid action. VVC, when persistent, frequent, or poorly responsive to therapy, was added as a clinical category B condition in the revised classification of clinical AIDS. These actions may well have been premature, if not inappropriate.

The controversy is whether VVC, particularly recurrent VVC, is more common in HIV-infected women than in matched control HIV-negative women and, if so, why [38]. Unfortunately, the controversy remains largely unresolved some 13 years later. Although several cross-sectional studies and even 2 large cohort studies were done in the early 1990s, these studies were not designed to measure incidental VVC. Thus, the true attack rate of VVC among HIV-infected women remains undetermined and is likely to vary substantially among Candida-colonized women, because symptomatic vaginitis depends upon a complex interaction of host, biological, and behavioral factors (i.e., hormonal status, antibiotic exposure, and to some extent, sexual behavior). Unfortunately, the widespread tendency to self-diagnose VVC (often incorrectly) and to self-treat will make data collection difficult, if not impossible.

Unlike traditional sexually transmitted pathogens, e.g., T. vaginalis, Neisseria gonorrhoeae, and herpes simplex virus, Candida albicans can be considered part of the normal flora and lacks the same public health epidemiological implications. VVC, in contrast to virtually all other lower-genital-tract infections, does not indicate unsafe sexual behavior, and the incidence of VVC is not likely to be affected by changes in behavior within the population.

One conclusion is undisputed, however: in HIV-infected women, VVC occurs far less frequently than oropharyngeal candidiasis [39]. The attack rate and recurrence of oropharyngeal candidiasis among women infected with HIV are extremely high and not different from those among males. Several studies have now consistently shown higher rates of vaginal Candida colonization among HIV-positive women [5, 9, 39–42]. In cross-sectional studies, HIV-negative women were carefully matched for HIV acquisition risk, race, and sexual behavior. Vaginal Candida colonization rates were still 40% lower than those of oropharyngeal colonization [39]. Rates of vaginal Candida colonization appear to increase with time and with progressive immunodeficiency [36].

Although it is tempting to view higher vaginal colonization rates as proof of higher attack rates of symptomatic vaginitis, this extrapolation is not justified since diagnosis of vaginitis requires, in addition to the presence of yeast, the consequent occurrence of symptoms such as pruritus and signs of inflammation (erythema, edema, and fissures). Moreover, transformation from asymptomatic colonization to symptomatic vaginitis requires exogenous factors such as antibiotic agents and sexual activity. It is worth noting that in the longitudinal cohort studies, VVC (as detected at scheduled routine physical examinations) has not been significantly more common among HIV-positive women [39].

Evidence of refractory VVC and vaginitis that do not respond to conventional antifungal therapy has also not been forthcoming. Similarly, although Spinillo [43] reported a higher frequency of non-albicans Candida species in HIV-seropositive women with recurrent VVC, other studies have not shown an increased prevalence of non-albicans Candida species among HIV-infected women [39]. Thus, the clinical and microbiological spectrum of VVC appears similar in HIV-positive and HIV-negative women, and treatment principles should be identical to those for HIV-negative women. Schuman et al. [44] demonstrated that suppressive prophylactic therapy with fluconazole (200 mg once weekly) effectively decreased recurrences of symptomatic VVC in HIV-positive women. Nevertheless, in spite of the efficacy and safety of this regimen, primary prophylaxis is expensive, unnecessary, and not recommended. One of the observations to emerge from this study was a tendency for Candida glabrata to replace C. albicans as a colonizing...
organism [44]. To date, azole resistance of *C. albicans* vaginal isolates has been rare, in contrast to resistance of isolates in cases of oropharyngeal candidiasis.

Whether candidal vaginitis with overt inflammation influences transmission of HIV and specifically increases susceptibility to HIV infection is unknown. In a recent prospective study of women in Tanzania, Kapiga et al. [41] found that the presence of VVC at the beginning of the period of observation conferred a relative risk for HIV seroconversion of 1.98 (95% CI, 1.17–3.33) and remained an independent risk factor in multivariate analysis. In a large pregnancy study, Burns et al. [42] concluded that VVC was not associated with an increased risk of mother-to-infant transmission of HIV.

**Genital Ulceration in HIV-Infected Women**

Many studies have reported an association between genital ulcer disease and acquisition of HIV; specifically, the role of genital ulcer disease in facilitating the transmission of HIV is well documented [45–51]. The association is particularly strong with genital herpes due to herpes simplex virus (HSV) and chancroid infection [46]. HSV and HIV share many sexual-behavior risk factors.

In addition to the usual causes of genital ulcers in women caused by *Treponema pallidum*, *HSV*, and *Haemophilus ducreyi*, a variety of other pathogens and pathogenic processes are reported to occur in HIV-seropositive women. Polymicrobial infections are more common, especially with chronic ulcers, and often involve the above pathogens together with cytomegalovirus (CMV), *Mycobacterium avium* complex in severely immunodeficient women [52], and adenovirus. More common is idiopathic culture-negative chronic ulceration of the vulva, vestibule, and vagina, which is accompanied by severe pain as well as sinus tract and fistula formation [53]. Idiopathic genital ulceration is resistant to anti-HSV therapy but may respond to systemic steroids, thalidomide, or antiretroviral therapy [53]. Foscarnet therapy has also rarely been causally associated with genital ulcers in males [54]. Because of the low accuracy of clinical diagnosis, multiple PCR analysis has been used to establish the etiology of ulcers, including the coexistence of multiple pathogens [52].

Genital herpes occurs more frequently in HIV-infected women than in uninfectected women, with more severe clinical expression and asymptomatic viral shedding correlated that is with severity of immunodeficiency [55–58]. The cumulative incidence of genital herpes in HIV-seropositive heterosexual women is high: 43% in a recent study in the United Kingdom [55], which is considerably higher than the incidence in the local STD clinic population. Large recalcitrant herpetica ulcers may be the initial HIV-related complaint and AIDS-defining illness. Similarly, HSV ulcers that persist for >1 month suggest AIDS-related immunodeficiency, as does the not-infrequent observation of resistance to acyclovir. Acyclovir resistance is best managed with intravenous foscarnet. Not all investigators have reported a particularly aggressive course for genital HSV infection in HIV-infected women [59]. Of note, several studies have reported that genital ulcer disease (GUD), particularly with ulcers due to HSV, promotes transmission of HIV [45, 49–51] because of a breakdown in epithelial integrity and the presence of CD4 lymphocytes that are attracted to the site. In addition, HIV-1 DNA is often isolated in genital ulcers [52] and HIV virions are shed in high titer for prolonged periods [60]. There is some evidence of a correlation between systemic HIV RNA load and HIV shedding from ulcers [61].

The presence of genital herpes is strongly associated with concordance of HIV infections among heterosexual couples, especially if both partners have herpes [62]. Effective therapy for genital herpes can potentially reduce the incidence of HIV and, together with treatment of other STDs, is the cornerstone of HIV prevention in many parts of the world [63]. Because of the possibility of asymptomatic recurrences, the true population-attributable risk of HIV infection related to genital herpes may be higher than for other causes of GUD [55]. In vitro studies by Heng et al. [57] demonstrated a synergistic relationship between HSV and HIV leading to enhanced replication of both viruses. It is not clear whether HSV genital infection influences the course of HIV disease; equally inconclusive are the minimal data that suggest improved survival rates for patients who receive high-dose acyclovir. HIV-seropositive women with proven HSV genital infection should be treated with anti–herpes virus agents, just as for HIV-negative women; the regimen should include the use of long-term suppressive therapy if clinically indicated.

**Cervicitis**

Given the fact that sexual behavior is a risk factor for HIV acquisition, it is not surprising that positive cervical cultures as well as mucopurulent cervicitis due to *N. gonorrhoeae* and *Chlamydia trachomatis* are common in HIV-seropositive women [64, 65]. In a cross-sectional study of prostitutes in Nairobi, Kreiss et al. [65] reported a correlation between macroscopic and microscopic evidence of cervicitis and cervical HIV shedding. In fact, the strongest predictor of cervical HIV detection was the presence of cervical inflammation [65]. In the same study population, both cervical ectopy and cervicitis were associated with increased viral shedding, although direct evidence of increased infectivity was unproven [58].

Several other investigators have confirmed the independent relationship between cervical HIV shedding and cervical mucopus [66–68], as well as the increased likelihood among HIV-infected women (versus matched HIV-seronegative control women) that swab specimens will be positive for *C. trachomatis* and *N. gonorrhoeae* [64]. The adjusted relative risk for HIV infection was found to be 3.3 (P < .05) in the presence of *C. trachomatis* cervical inflammation among female sex workers.
in Thailand [47]. Taha et al. [22] found HIV seroconversion rates of 0.1% for pregnant Malawi women without gonorrhea and 2.62% for women with gonorrhea (RR, 2.96; no significant difference).

Increased HIV shedding is thought to be the consequence of inflammatory cell recruitment to cervical mucosa, which increases the concentration of HIV-infected CD4 lymphocytes and infected monocytes/macrophages [69]. Moreover, in the presence of inflammation, HIV replication is enhanced by local cytokines. Cohen et al. [70] detected an increase in IL-10 in the cervical secretions of women with gonorrhea, chlamydia, and trichomoniasis. IL-10 regulates the expression of the chemokine receptor CCR5 and increases the efficiency of HIV infection of macrophages in vitro. Finally, micro-ulceration and friable hemorrhagic mucosa provide a portal of exit and entry for HIV virus or infected cells [67].

Bacterial cervicitis may cause a purulent discharge but is usually asymptomatic, occasionally presenting as acute pelvic inflammatory disease (PID). HIV-seropositive women with chlamydial or gonococcal cervical infection have a greater risk of premature delivery and chorioamnionitis, which in itself is associated with perinatal HIV transmission, although overall vertical HIV transmission has not been correlated with chlamydia or the presence of N. gonorrhoeae in the cervix [64]. Treatment of cervicitis should follow the standard guidelines for HIV-seronegative women.

Pelvic Inflammatory Disease

PID is a severe and common complication of STDs in women and is associated with serious sequelae, including chronic lower abdominal pain, tubal infertility, and ectopic pregnancy. Since the epidemic of HIV infection is concentrated in populations with a high incidence of traditional STDs [74], HIV seropositivity is not infrequent in hospitalized women with acute PID, ranging from 8% in Brooklyn to 15%–29% in sub-Saharan Africa [75–77]. These studies indicate that PID is more common in women infected with HIV and is recognized as justification for HIV testing when serostatus is unknown.

Studies of the influence of HIV disease on the presentation and clinical course of PID in various settings have produced some similar and some disparate findings. Most investigators found that HIV-seropositive females presented with high febrile temperatures and low leukocyte counts [75, 78]. Although some investigators found a higher frequency of complicating tubo-ovarian abscesses formation [75, 78–80], together with a greater need for change in therapy or surgical intervention [75, 78, 79], others found the frequency of neither was increased. Most studies showed the predicted response to recommended antibiotic therapy was reasonably similar for HIV-positive and HIV-negative women [70]. Similarly, the microbiology of organisms identified is similar, although the incidence of N. gonorrhoeae and C. trachomatis in developed countries appears low [70–72, 78, 79].

Since the majority of HIV-positive women with acute PID are not severely immunodeficient, numbers of women with PID and low CD4 lymphocyte counts are few; hence, the impact of immunodeficiency or clinical disease is not apparent. Recently, Cohen et al. [70] reported that the increased risk of tubo-ovarian abscess formation was related to severity of immunodeficiency. These data support the CDC recommendations that HIV-infected women with PID receive initial inpatient therapy with standard antibiotic regimens. Since the use of intrauterine devices (IUDs) is recognized as an independent risk factor for acute PID in women, concern has been raised about use of these devices in HIV-positive women who may have no other means of contraception [81]. Recently, however, Sinei et al. [82], working with a World Health Organization expert group, concluded that IUDs may be safe contraceptives for appropriately selected HIV-1-infected women with ongoing access to medical services.

Cytomegalovirus Infections of the Genital Tract

Whereas the incidence of CMV infection of the female genital tract has been reported to vary from 4% to 12% among healthy HIV-negative women, little information is available on its incidence among HIV-seropositive women, although retinal or gastrointestinal infection is common, especially in severely immunocompromised women [71]. Age <30 years and increased sexual activity have been associated with higher rates of genital CMV infection, as measured by positive cultures [71]. Most women with genital tract CMV excretion are largely asymptomatic. Infrequent reports of symptomatic infection have appeared to include vulvar ulceration (often mixed, polymicrobial); painful vaginal ulceration; and cervical inflammation that is characterized by an elevated number of polymorphonuclear leukocytes, CMV-positivity of a cervical swab culture, and presence of intranuclear inclusions consistent with CMV on a Papnicolaou smear [72]. There have been rare reports of febrile HIV-seropositive patients with clinical manifestations of PID who failed to respond to antibacterial agents but appeared to benefit from ganciclovir therapy after CMV was found in genital secretions [73].
HPV carriage also was correlated with plasma viral load. In addition, HIV-positive women are more likely to simultaneously carry multiple HPV types [87], have higher-intensity HPV infection [88], and have longer carriage or persistence of HPV in cervical specimens [85], including the types of HPV that are strongly associated with the development of high-grade squamous intraepithelial lesions and invasive cervical cancer. Ellerbrock et al. [86] reported that about 20% of HIV-infected women in New York City developed cervical squamous intraepithelial lesions over a 3-year period, a finding that emphasizes the importance of cervical cancer screening programs in this population. This study was performed before the widespread availability of antiretroviral combination therapy. None of the women in the study had evidence of squamous intraepithelial lesions at baseline. The incidence of biopsy-confirmed squamous intraepithelial lesions among HIV-infected women was 8.3 per 100 person-years of follow-up, compared with 1.8 per 1000 person-years among uninfected women [86]. Other risk factors for HPV infection in HIV-positive women include black race, current smoking, and age <30 years.

Both low-grade and high-grade squamous intraepithelial lesions of the cervix are strongly associated with HIV seropositivity and immunosuppression [88–90]. Cervical abnormalities were noted in 16% of HIV-negative and 53% of HIV-positive women with CD4 lymphocyte counts <200 cells/mm³, and low-grade squamous intraepithelial lesions were found in 14.1% of women with CD4 lymphocyte counts >400 cells/mm³, and 41.9% of women with lower CD4 lymphocyte counts (P < .001) [88, 89].

It has been suggested that the HIV protein tat may upregulate production of HPV proteins E6 and E7 in HPV-infected cells [91, 92]. These HPV proteins are thought to regulate normal mammalian oncogene suppression. Although the association between HIV infection and invasive carcinoma of the cervix has long been suspected, several studies have failed to confirm an increase in invasive cervical cancer among women with a high prevalence of HIV infection [84, 89, 91]. A possible explanation is the long interval required for the conversion of high-grade squamous intraepithelial lesions to invasive cervical cancer [89], coupled with the short life-expectancy of HIV-infected women [79, 84, 87, 89, 93]. It is generally believed that when invasive cervical cancer does develop, its progression is rapid, and in the presence of severe immunodeficiency due to HIV the course may be aggressive [91]. To date, highly active antiretroviral therapy has not been shown to reverse the course of cervical dysplastic changes [94].

**Syphilis**

Clinical manifestations in the genital tract appear similar in HIV-positive and HIV-negative women, although more florid manifestations are seen in HIV-positive women. Tests for *T. pallidum* are essential in the differential diagnosis of vulvar, vaginal, and cervical lesions, including ulcers [52]. *T. pallidum* may coexist with other STD pathogens. The diagnosis of syphilis is more complicated for HIV-infected women. False-positive serological tests are more common, possibly because of HIV-induced polyclonal activation. Similarly, the serological response to conventional therapy may be slower, and false-negative results of fluorescent treponemal antibody (absorbed) tests have been reported. Vertical transmission of maternal HIV to the fetus seems to be more common in the presence of active syphilis, regardless of stage of the latter [95] and possibly related to treponemal inflammation of the placenta. Treatment principles follow the guidelines for HIV-negative women, although concerns about a higher syphilis relapse rate have been raised [96].

References


