

HIV CareLink

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Practical Guide to the Management of Gynecological Problems in HIV-Infected Women

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Women represent an increasing percentage of all acquired immunodeficiency syndrome (AIDS) cases in the United States and worldwide.¹ Although many of the manifestations of HIV infection in women are similar to those in men, there are some important gender-based differences such as viral loads, AIDS-related mortality, barriers to care and depression. HIV-infected women are at increased risk of abnormal cervical cytology, cervical cancer, recurrent vaginal candidiasis and vaginitis, menstrual disorders, pelvic inflammatory disease, genital ulcers and sexually transmitted diseases. Contraception and emergency contraception can also be challenging in HIV-infected patients.

Cervical dysplasia and cervical cancer

- HIV-infected women are at a higher risk of developing cervical dysplasia and cervical cancer.
- Immunosuppression plays an important role in increasing the virulence of human papillomavirus (HPV) leading to more cervical dysplasia and cervical cancer in these patients.
- Women with CD4+ count <200 cells/mm³ have a higher prevalence of high-risk HPV infection, higher risk of persistence of cervical HPV infection and lower rate of regression of untreated low grade cervical intraepithelial neoplasia (CIN) compared to women with CD4+ count > 500 cells/mm^{3,2,3,4}
- CDC considers moderate and severe CIN as conditions defining a stage of early symptomatic HIV infection and invasive cervical cancer as an AIDS-defining condition.⁵
- Screening for cervical cancer and management of cervical dysplasia in HIV-infected patients should take into consideration the CD4+ count, HAART therapy and HPV status. For a more detailed discussion of screening recommendations, please refer to *Guidelines for Preventing Opportunistic Infections Among HIV-Infected Persons - 2002* (<http://www.aegis.com/PUBS/mmwr/2002/rr5108a1.html>).

- There is no contraindication to the use of the HPV vaccine Gardasil® in HIV-infected and immunosuppressed individuals; however, there are no clinical data on its efficacy in this patient population.⁶
- There is no clinical data on the efficacy of the HPV vaccine as treatment of an established HPV infection in HIV-infected individuals, and very limited data in immunocompetent individuals.

Vulvovaginal Candidiasis

- Vulvovaginal candidiasis occurs with higher incidence and greater persistence, but not greater severity in HIV-infected women.⁷
- Infections in HIV-infected patients are complicated and require more aggressive treatment to achieve relief of symptoms.⁸
- Fluconazole 150 mg one dose, followed by a second dose 3 days later is recommended.
- For recurrent vulvovaginal candidiasis secondary to *C. albicans*, an initial intensive therapy for 7-14 days (topical imidazoles or oral fluconazole) to achieve remission followed by fluconazole 150 mg weekly for 6 months is recommended.
- In pregnancy, topical imidazoles for 7 days are recommended, rather than oral fluconazole.

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ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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Bacterial Vaginosis and Trichomoniasis

- HIV-infected women have similar incidence of bacterial vaginosis and vaginal trichomonas as HIV-negative patients.⁹
- HIV-infected patients with bacterial vaginosis or trichomoniasis can be treated with standard treatment protocols.
- Bacterial vaginosis: metronidazole 500 mg twice daily for 7 days.
- Trichomoniasis: metronidazole 500 mg 4 tabs (2000 mg) once or 500 mg twice daily for 7 days are recommended for both, the patient and her sexual partner.

Sexually Transmitted Diseases

- It has been shown that STDs in an HIV-exposed or HIV-infected individual enhance the rate of transmission of HIV.¹⁰
- Treating STDs in HIV-infected individuals may be a simple and cost-effective method of decreasing the transmission and incidence of HIV infections especially in resource limited and developing countries.
- The CDC recommends routine screening for curable STDs (such as syphilis, gonorrhea, and chlamydia) at least yearly for sexually active persons and aggressive treatment of STDs in HIV-infected individuals.

Pelvic Inflammatory Disease (PID)

- HIV-infected patients with PID have similar symptoms to HIV-negative controls.
- Are more likely to have a tubo-ovarian abscess.
- Respond equally well to the standard recommended antibiotic regimens.
- The indications for hospitalization or parenteral antibiotics should follow the standard recommendations for PID patients that are HIV-negative.

Use of Contraception and Emergency Contraception

- Health care providers should have comprehensive knowledge of the different methods of contraception in this special population of patients in order to help them make informed and appropriate decisions regarding reproductive planning.
- Choosing the proper contraceptive should take into consideration the method, its efficacy, prevention of transmission of HIV or other STDs, and the drug interaction between hormonal contraceptives and antiretroviral medications.
- A barrier form of contraception is always recommended to decrease the risk of HIV and other STD transmission, irrespective of the viral load or CD4+ count.
- Some experts recommend dual contraception with a barrier method, such as condoms, to decrease HIV and other STD transmission and hormonal method to prevent pregnancy.¹¹
- Vaginal spermicides containing nonoxynol-9 (N-9) or condoms lubricated by N-9 are not recommended for STD/HIV prevention since they have been associated with disruption of the vaginal epithelium which might be associated with a higher risk of HIV transmission.

- As for emergency contraception using Levonorgestrel (Plan B®), the recommendation for patients on enzyme inducers (PI or NNRTI) is 2 tablets (1.5 mg) followed by 1 tablet (0.75 mg) 12 hours later.¹¹ The recommended usual dose (i.e., when there are no drug-drug interactions) is Levonorgestrel 1 tablet (0.75 mg) x 2 doses 12 hours apart or 1.5 mg single dose within 72 hours of unprotected intercourse.¹²

Menstrual Irregularities and Menopause

- Menstrual irregularities in HIV-infected patients have been described, but the patterns, rates, and etiology have not been well characterized.
- A study comparing characteristics of menstruation in HIV-infected women to uninfected controls found no difference in patterns of bleeding (intermenstrual bleeding, postcoital bleeding or no bleeding) between the 2 groups; neither HIV infection, nor immunosuppression had any clinically relevant effect on menstruation or other vaginal bleeding.¹³
- Standard evaluation and treatment for menstrual irregularities is warranted in HIV-infected women.
- HIV infection and immunosuppression are associated with the onset of menopause at an earlier age.¹⁴
- Standard education and counseling about menopause are recommended.

Assisted Reproduction and Infertility Treatment

- HIV-infected patients are living longer and a growing proportion are thinking about childbearing.
- Many turn to infertility clinics seeking ways that may avoid putting themselves or their partner at risk of acquiring HIV or new viral strain.
- Prior to attempting any assisted reproductive technology (ART), the HIV status of the patient should be optimized by the HIV specialist taking care of this patient.
- The patient should have a strong desire to have a child and options include: ART (intrauterine insemination, in-vitro fertilization, and intracytoplasmic sperm injection), donor sperm and adoption.
- Pre-conception counseling is strongly recommended for any couple with one or both partners being HIV positive.

¹Hader SL; Smith DK; Moore JS; Holmberg SD. HIV infection in the United States: status at the Millennium. *JAMA* 2001 Mar 7;285(9):1186-92

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⁴Delmas MC; Larsen C; van Benthem B; et al. Cervical squamous intraepithelial lesions in HIV-infected women: prevalence, incidence and regression. *European Study Group on Natural History of HIV Infection in Women. AIDS* 2000 Aug 18; 14(12):1775-84

⁵From the Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *JAMA* 1993 Feb 10; 269(6):729-30

⁶Human papillomavirus vaccination. ACOG Committee Opinion No. 344. *American College of Obstetricians and Gynecologists. Obstet Gynecol* 2006;108:699-705

⁷Duerr A; Heilig CM; Meikle SF; et al. Incident and persistent vulvovaginal candidiasis among human immunodeficiency virus-infected women: Risk factors and severity. *Obstet Gynecol* 2003 Mar; 101(3): 548-56

⁸ACOG Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin. Clinical management guidelines for obstetricians-gynecologists, Number 72. May 2006:Vaginitis. *Obstet Gynecol*. 2006 May; 107(5):1195-1206

⁹Watts DH; Springer G; Minkoff H; et al. The occurrence of vaginal infections among HIV-infected and high-risk HIV-uninfected women: longitudinal findings of the women's interagency HIV study. *J Acquir Immune Defic Syndr*. 2006 Oct 1;43(2):161-8

¹⁰Kreiss J; Carael M; Meheus A. Role of sexually transmitted disease in transmitting human immunodeficiency virus. *Genitourin Med* 1988;64:1-2

¹¹Mitchell HS; Stephens E. Contraception choice for HIV positive women. *Sex Transm Infect* 2004;80:167-173

¹²Von Hertzen H; Piaggio G; Ding J; et al. Low dose Mefepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicenter randomized trial. *Lancet* 2002;360:1803-10

¹³Ellerbrock TV; Wright TC; Bush TJ; et al. Characteristics of menstruation in women infected with human immunodeficiency virus. *Obstet Gynecol* 1996 Jun;87(6): 1030-4

¹⁴Schoenbaum EE; Hartel D; Lo Y; et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis* 2005 Nov 15; 41(10):1517-24

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Changes Made to Sustiva® and Fuzeon® Product Labeling

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- Detailed information regarding changes posted by the FDA on 1/31/07 <http://www.fda.gov/oashi/aids/listserve/listserve2007.html#13107>

• Sustiva® Labeling Changes

- Drug interaction section updated to include updated information regarding interactions with diltiazem, itraconazole, voriconazole, atorvastatin, pravastatin, simvastatin
- Efavirenz ↓ levels of drugs listed above; additionally, voriconazole significantly ↑ efavirenz levels
 - When voriconazole and efavirenz are combined, voriconazole maintenance dose should be ↑ to 400 mg po q12h and efavirenz dose should be ↓ to 300 mg po qhs (using capsule formulation, tablets should not be broken)
- Contraindication section updated to include bepridil, pimozide, and voriconazole (at standard doses)
- Precaution section regarding drug interactions updated
 - Diltiazem—due to ↓ diltiazem levels (AUC ↓ 69%, active metabolites also ↓) dose should be guided by clinical response
 - Other calcium channel blockers—potential for efavirenz to ↓ levels, dose should be guided by clinical response
 - Itraconazole—consider alternative antifungal
 - Ketoconazole—not studied, efavirenz may ↓ ketoconazole levels, proper dose when combined not established
 - Rifampin—Dosing recommendations not established (efavirenz AUC ↓ 26%, unknown clinical significance)

• Fuzeon® Labeling Changes

- Product information updated to include safety information regarding Biojector® 2000 Needle-Free device
 - Precaution/adverse effect section updated to warn regarding potential for nerve pain (possibly lasting up to 6 months) when administered at sites where large nerves course close to the skin; administration section updated with the following statement:
 - “FUZEON should not be injected near any anatomical areas where large nerves course close to the skin, such as near the elbow, knee, groin or the inferior or medial section of the buttocks, skin abnormalities (including directly over a blood vessel, into moles, scar tissue, bruises) near the navel, surgical scars, tattoos or burn sites.”
- Bruising and hematomas have also been seen (patients on anticoagulants or those with bleeding disorders may be at increased risk)

Microbicide Trial Stopped

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- 2 trials using the compound cellulose sulfate as a potential microbicide to prevent HIV infection stopped early due to safety concerns
- The study that led to stopping the trials involved 1,333 participants in Benin, South Africa and Uganda. An independent review committee found more new HIV infections among those who used cellulose sulfate than among those who used placebo gel (detailed information to be released in March)
- A second study involving 1,700 participants in Nigeria found neither a benefit nor an increased risk

- In 2000, a prior study of another microbicide candidate, nonoxynol-9, showed that it increased risk of developing HIV infection likely through ulcers caused by chemical irritation from the product
- Three additional microbicide candidates are undergoing full scale testing
- Additional information available online at <http://www.un.org/apps/news/story.asp?NewsID=21407>

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