Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Postpartum Care

Postpartum Follow-Up of HIV-Infected Women (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations
• Contraceptive counseling should be included in the prenatal period as well as immediately postpartum as a critical aspect of postpartum care **(AIII)**.
• Decisions about continuing antiretroviral (ARV) drugs after delivery should take into account current recommendations for initiation of antiretroviral therapy (ART), current and nadir CD4 T-lymphocyte counts and trajectory, HIV RNA levels, adherence issues, whether a woman has an HIV-uninfected sexual partner, and patient preference **(AIII)**.
• For women continuing ARV drugs postpartum, arrangements for new or continued supportive services should be made before hospital discharge because the immediate postpartum period poses unique challenges to adherence **(AII)**.
• Women with a positive rapid HIV antibody test during labor require immediate linkage to HIV care and comprehensive follow-up, including confirmation of HIV infection. If infection is confirmed, a full health assessment is warranted, including evaluation for associated medical conditions, counseling related to newly diagnosed HIV infection, and assessment of need for ART and opportunistic infection prophylaxis **(AII)**.
• Breastfeeding is not recommended for HIV-infected women in the United States, including those receiving ART **(AII)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The postpartum period provides an opportunity to review and optimize women's health care. Comprehensive care and support services are particularly important for women with HIV infection and their families, who often face multiple medical and social challenges. Components of comprehensive care include the following medical and supportive care services as needed:

- primary, gynecologic/obstetric, and HIV specialty care for an HIV-infected woman;
- pediatric care for her infant;
- family planning services;
- mental health services;
- substance abuse treatment;
- support services; and
- coordination of care through case management for a woman, her child(ren), and other family members.

Support services should be tailored to individual women's needs and can include case management; child care; respite care; assistance with basic life needs, such as housing, food, and transportation; peer counseling; and legal and advocacy services. Ideally, this care should begin before pregnancy and continue throughout pregnancy and the postpartum period.

During the postpartum period, maternal medical services must be coordinated between obstetric care providers and HIV specialists. It is especially critical to ensure continuity of the antepartum antiretroviral (ARV) drug regimen when such treatment is required for a woman's health. The decision about whether to continue ARV drugs after delivery should be discussed with a woman and made before delivery.

The postpartum period also is a critical time for addressing the issue of safer sex practices, secondary transmission prevention, and contraception. It is important that comprehensive family planning and preconception care be integrated into routine health visits. Women who receive family planning counseling during prenatal care are more likely to use effective contraception postpartum.[1] Lack of breastfeeding is associated with earlier return of fertility; ovulation returns as early as 6 weeks postpartum, and even earlier in some women, putting them at risk of pregnancy shortly after delivery.[2] Interpregnancy intervals of less than 18 months have been associated with increased risk of poor perinatal and maternal outcomes in HIV-uninfected women.[3] Because of the stresses and demands of a new baby, women may be more receptive to use of effective contraception, yet simultaneously at higher risk of nonadherence to contraceptive use and, thus, unintended pregnancy.[4] This is an important concern in women who are on an efavirenz-containing regimen because of the potential risk of teratogencity in the first 5 to 6 weeks of pregnancy (the neural tube closes at 36–39 days after the last menstrual period). A "dual-protection" strategy, such as use of condoms plus a second highly effective contraceptive, is ideal for HIV-infected women because it provides simultaneous protection against unintended pregnancy, transmission of HIV, and acquisition or transmission of sexually transmitted disease.[5] Longer term reversible contraceptive methods, such as injectables, implants, and intrauterine devices (IUDs) should be included as options.

Drug interactions have been documented between oral contraceptives and many ARV drugs (see Table 4 in Preconception Counseling and Care for HIV-Infected Women of Childbearing Age); however, data primarily come from pharmacokinetic (PK) studies and the clinical implications have not been well studied. The magnitude of changes in contraceptive drug levels that may reduce contraceptive efficacy or increase contraceptive-associated adverse effects is unknown. Hormonal contraceptives can be used with antiretroviral therapy (ART) in women who have no other contraindications. Additional or alternative methods of contraception can be recommended where drug interactions are known. Estrogen-containing hormonal contraceptives significantly lower levels of amprenavir/fosamprenavir and, therefore, coadministration is not recommended. Whether low-dose ritonavir boosting raises amprenavir levels sufficiently to allow coadministration is unknown. Depot medroxyprogesterone acetate (Depo-Provera, DMPA) PKs are not significantly affected by nevirapine, efavirenz, or nelfinavir and levels of these drugs were not significantly altered by DMPA.[6] Adverse effects of DMPA are no different in HIV-infected women on ARV drugs than in HIV-uninfected women.[7] In one study, DMPA use was associated with an increase in acquisition of HIV by uninfected women and transmission of HIV from infected women to male partners, but other studies have not seen this association and further studies are needed.[8] Other non-oral contraceptives, such as levonorgestrel implants, the combined contraceptive patch, the combined hormonal contraceptive vaginal ring, and the levonorgestrel IUD, are largely unstudied in combination with ARV drugs, but some data do exist on lopinavir/ritonavir interactions with the estrogen patch.[9] ARV drug interactions may be of less concern with contraceptive methods that exert primarily local activity and have minimal systemic absorption, but there is still potential for interaction if metabolic or elimination pathways are shared.[6, 10] The World Health Organization has summarized the research on hormonal contraception, IUD use, and risk of HIV infection.[11] Permanent sterilization is appropriate only for women who are certain they do not desire future childbearing.

Decisions about whether to continue ARV drugs after delivery should be made in consultation with the HIV provider. Factors to be taken into consideration should include current recommendations for initiation of ART, current and nadir CD4-lymphocyte counts and trajectory, HIV RNA levels, adherence issues, partner HIV status, and patient preference. Women with nadir CD4 T-lymphocyte (CD4-cell) counts less than the currently recommended threshold for institution of ART[12] and/or symptomatic HIV infection should be encouraged to continue their ARV regimens postpartum without interruption. The risks versus benefits of stopping combination ART drug regimens postpartum in women with high CD4-cell counts are being evaluated in the ongoing PROMISE study (clinical trial number NCT00955968). Unplanned changes in ARV

regimens and discontinuations of ART in the postpartum period have led to viral load rebound.[4]

Recent data from the HPTN 052 clinical trial showed that earlier initiation of ARV drugs led to a significant reduction in sexual transmission of HIV to uninfected partners in serodiscordant couples (see Preconception Counseling). HPTN 052 evaluated immediate versus delayed initiation of ART to HIV-infected individuals with CD4-cell counts between 350 and 550 cells/mm^3. Based on the results from that trial, continued administration of ARV drugs may be recommended for prevention of sexual transmission of HIV in postpartum women who have CD4-cell counts between 350 and 550 cells/mm^3 and have HIV-uninfected sexual partners, and it can be considered for those with CD4-cell counts greater than 550 cells/mm^3 with HIV-uninfected sexual partners. It is important to counsel the woman that no single method (including treatment of the infected partner) is fully protective against HIV transmission and safer sexual practices should be continued.

Concerns have been raised about adherence to ARV regimens during the postpartum period, because a number of studies have found significant decreases in adherence postpartum.[13-16] Women should be counseled that postpartum physical and psychological changes and the stresses and demands of caring for a new baby may make adherence more difficult and that additional support may be needed during this period.[17-19] Health care providers should be vigilant for signs of depression and illicit drug or alcohol use that may require assessment and treatment and interfere with adherence. Poor adherence has been shown to be associated with virologic failure, development of resistance, and decreased long-term effectiveness of ART.[20-22] Simplification of an ARV regimen (for example, to once-daily medications) can be considered. It may be preferable to temporarily interrupt ART in women who are unable to adhere to their regimens while they work with a provider on strategies to improve adherence. Efforts to maintain adequate adherence during the postpartum period may prolong the effectiveness of therapy (see the section on *Adherence* in the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*).

For women whose antepartum regimen included a non-nucleoside reverse transcriptase inhibitor (NNRTI) and who plan to stop ARV prophylaxis after delivery, consideration should be given to stopping the NNRTI and continuing the other ARV drugs for a period of time before stopping electively. The optimal interval between stopping an NNRTI and the other ARV drugs is unknown; a minimum of 7 days is recommended. Because efavirenz-based therapy has potential to result in prolonged, detectable NNRTI concentrations for more than 3 weeks, some experts recommend that patients receiving efavirenz continue their other ARV drugs or substitute a protease inhibitor (PI) for the NNRTI drug in combination with their other ARV drugs for up to 30 days after stopping efavirenz (see Stopping Antiretroviral Therapy during Pregnancy and Prevention of Antiretroviral Drug Resistance). Women whose antepartum regimen did not include an NNRTI and who plan to stop ARV prophylaxis after delivery should stop all ARV drugs at the same time. Doses of some PIs may be increased during pregnancy. For women continuing therapy, available data suggest that standard doses can be used again, beginning immediately after delivery.

Immediate linking to care, comprehensive medical assessment, counseling, and follow-up are required for women who test positive on rapid HIV antibody assay during labor or at delivery. To minimize the delay in definitive diagnosis, confirmatory HIV antibody testing should be performed as soon as possible after an initial positive rapid test.[23] Women who test positive on rapid HIV antibody assay should not breastfeed unless a confirmatory HIV test is negative. Women with a new HIV diagnosis postpartum should receive the same thorough evaluation as other newly identified infected patients, including consideration of ART and prophylaxis for opportunistic infections, as indicated. Other children and partner(s) should be referred for HIV testing.

References

1. Jackson E. Controversies in postpartum contraception: when is it safe to start oral contraceptives after childbirth? *Thromb Res*. Feb 2011;127(Suppl 3):S35-39. Available at http://www.ncbi.nlm.nih.gov/pubmed/21262436.

2. Jackson E, Glasier A. Return of ovulation and menses in postpartum nonlactating women: a systematic review. *Obstet Gynecol*. Mar 2011;117(3):657-662. Available at http://www.ncbi.nlm.nih.gov/pubmed/21343770.

3. Sholapurkar SL. Is there an ideal interpregnancy interval after a live birth, miscarriage or other adverse pregnancy outcomes? *J Obstet Gynaecol*. Feb 2010;30(2):107-110. Available at http://www.ncbi.nlm.nih.gov/pubmed/20143964.

4. Sha BE, Tierney C, Cohn SE, et al. Postpartum viral load rebound in HIV-1-infected women treated with highly active antiretroviral therapy: AIDS Clinical Trials Group Protocol A5150. *HIV Clin Trials*. Jan-Feb 2011;12(1):9-23. Available at http://www.ncbi.nlm.nih.gov/pubmed/21388937.

5. Cates W, Jr., Steiner MJ. Dual protection against unintended pregnancy and sexually transmitted infections: what is the best contraceptive approach? *Sex Transm Dis*. Mar 2002;29(3):168-174. Available at http://www.ncbi.nlm.nih.gov/pubmed/11875378.

6. Cohn SE, Park JG, Watts DH, et al. Depo-medroxyprogesterone in women on antiretroviral therapy: effective contraception and lack of clinically significant interactions. *Clin Pharmacol Ther*. Feb 2007;81(2):222-227. Available at http://www.ncbi.nlm.nih.gov/pubmed/17192768.

7. Watts DH, Park JG, Cohn SE, et al. Safety and tolerability of depot medroxyprogesterone acetate among HIV-infected women on antiretroviral therapy: ACTG A5093. *Contraception*. Feb 2008;77(2):84-90. Available at http://www.ncbi.nlm.nih.gov/pubmed/18226670.

8. Heffron R, Donnell D, Rees H, et al. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. *Lancet Infect Dis*. Jan 2012;12(1):19-26. Available at http://www.ncbi.nlm.nih.gov/pubmed/21975269.

9. Vogler MA, Patterson K, Kamemoto L, et al. Contraceptive efficacy of oral and transdermal hormones when co-administered with protease inhibitors in HIV-1-infected women: pharmacokinetic results of ACTG trial A5188. *J Acquir Immune Defic Syndr*. Dec 2010;55(4):473-482. Available at http://www.ncbi.nlm.nih.gov/pubmed/20842042.

10. Womack J, Williams A. Hormonal contraception in HIV-positive women. *AIDS Read*. Jul 2008;18(7):372-377, 381. Available at http://www.ncbi.nlm.nih.gov/pubmed/18655314.

11. World Health Organization. Review of Priorities in Research on Hormonal Contraception and IUDs and HIV Infection. 2010; Geneva. Available at http://whqlibdoc.who.int/hq/2010/WHO_RHR_10.21_eng.pdf. Accessed on June 29, 2012.

12. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed on June 29, 2012.

13. Kreitchmann R, Harris DR, Kakehasi F, et al. Antiretroviral Adherence During Pregnancy and Postpartum in Latin America. *AIDS Patient Care STDS*. Jun 4 2012. Available at http://www.ncbi.nlm.nih.gov/pubmed/22663185.

14. Kaida A, Kanters S, Chaworth-Musters T, et al. Antiretroviral adherence during pregnancy and postpartum among HIV-positive women receiving highly active antiretroviral therapy (HAART) in British Columbia (BC), Canada (1997-2008). Paper presented at: 6th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention; July 17-20, 2011; Rome, Italy. Abstract CDB397-CD-ROM.

15. Mellins CA, Chu C, Malee K, et al. Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS Care*. Sep 2008;20(8):958-968. Available at http://www.ncbi.nlm.nih.gov/pubmed/18608073.

16. Nachega J, Uthman C, Mills E, Muessig K, et al. Adherence to antiretroviral therapy (ART) during and after pregnancy in low, middle and high income countries: a systematic review and meta-analysis. Paper presented at: 19th Conference on Retroviruses and Opportunistic Infections (CROI); March 5-8, 2012; Seattle, WA. Abstract 1006.

17. Cohn SE, Umbleja T, Mrus J, Bardeguez AD, Andersen JW, Chesney MA. Prior illicit drug use and missed prenatal vitamins predict nonadherence to antiretroviral therapy in pregnancy: adherence analysis A5084. *AIDS Patient Care STDS*. Jan 2008;22(1):29-40. Available at http://www.ncbi.nlm.nih.gov/pubmed/18442305.

18. Ickovics JR, Wilson TE, Royce RA, et al. Prenatal and postpartum zidovudine adherence among pregnant women with HIV: results of a MEMS substudy from the Perinatal Guidelines Evaluation Project. *J Acquir Immune Defic Syndr*. Jul 1 2002;30(3):311-315. Available at http://www.ncbi.nlm.nih.gov/pubmed/12131568.

19. Bardeguez AD, Lindsey JC, Shannon M, et al. Adherence to antiretrovirals among US women during and after pregnancy. *J Acquir Immune Defic Syndr*. Aug 1 2008;48(4):408-417. Available at http://www.ncbi.nlm.nih.gov/pubmed/18614923.

20. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med*. Jul 4 2000;133(1):21-30. Available at http://www.ncbi.nlm.nih.gov/pubmed/10877736.

21. Le Moing V, Chene G, Carrieri MP, et al. Clinical, biologic, and behavioral predictors of early immunologic and virologic response in HIV-infected patients initiating protease inhibitors. *J Acquir Immune Defic Syndr.* Aug 1 2001;27(4):372-376. Available at http://www.ncbi.nlm.nih.gov/pubmed/11468425.

22. Murri R, Ammassari A, Gallicano K, et al. Patient-reported nonadherence to HAART is related to protease inhibitor levels. *J Acquir Immune Defic Syndr*. Jun 1 2000;24(2):123-128. Available at http://www.ncbi.nlm.nih.gov/pubmed/10935687.

23. Centers for Disease Control and Prevention (CDC). Rapid HIV-1 antibody testing during labor and delivery for women of unknown HIV status: a practical guide and model protocol. 2004. Available at http://www.cdc.gov/hiv/topics/testing/resources/guidelines/pdf/Labor&DeliveryRapidTesting.pdf. Accessed July 3, 2012.