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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Special Situations — HIV-2 Infection and Pregnancy (Last updated July 31, 2012; last reviewed July 31, 2012)

Panel's Recommendations

- HIV-2 infection should be suspected in pregnant women who are from—or have partners from—countries in which the disease is endemic, who are HIV antibody positive on an initial enzyme-linked immunoassay screening test, and who have repeatedly indeterminate results on HIV-1 Western blot along with HIV-1 RNA viral loads at or below the limit of detection **(BII)**.
- A regimen with two nucleoside reverse transcriptase inhibitors (NRTIs) and a boosted protease inhibitor (PI) currently is recommended for HIV-2-infected pregnant women who require treatment for their own health because they have significant clinical disease or CD4 T-lymphocyte (CD4-cell) counts <500 cells/mm^3 **(AIII)**.
  - Based on available data on safety in pregnancy, zidovudine/lamivudine plus lopinavir/ritonavir would be preferred **(AIII)**. Tenofovir plus lamivudine or emtricitabine plus lopinavir/ritonavir can be considered as an alternative **(BIII)**.
- Optimal prophylactic regimens have not been defined for HIV-2-infected pregnant women who do not require treatment for their own health (that is, CD4-cell counts >500 cells/mm^3 and no significant clinical disease). Experts have recommended the following approaches:
  - A boosted PI-based regimen (two NRTIs plus lopinavir/ritonavir) for prophylaxis, with the drugs stopped postpartum **(BIII)**; or
  - Zidovudine prophylaxis alone during pregnancy and intrapartum **(BIII)**.
- Non-nucleoside reverse transcriptase inhibitors and enfuvirtide are not active against HIV-2 and should not be used for treatment or prophylaxis **(AIII)**.
- All infants born to HIV-2-infected mothers should receive the standard 6-week zidovudine prophylactic regimen **(BIII)**.
- In the United States, breastfeeding is not recommended for infants of HIV-2-infected mothers **(AIII)**.

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*

HIV-2 infection is endemic in West African countries including Ivory Coast, Ghana, Cape Verde, Gambia, Mali, Senegal, Liberia, Guinea, Burkina Faso, Nigeria, Mauritania, Sierra Leone, Guinea Bissau, Niger, Sao Tome, and Togo; Angola; Mozambique; and in parts of India.[1-3] It also occurs in countries such as France and Portugal, which have large numbers of immigrants from these regions.[3, 4] HIV-2 is rare in the United States. Between 1998 and 2010, a total of 242 HIV-2 cases were reported to the Centers for Disease Control and Prevention (CDC), with 166 cases meeting criteria for HIV-2 diagnosis. These 166 cases constituted only 0.01% of the more than 1.4 million U.S. cases of HIV infection.[5] Of the 50 women aged 15 to 44 years at diagnosis, 24 (48%) were pregnant at or after HIV-2 diagnosis.[5] HIV-2 infection should be suspected in pregnant women who are from—or who have partners from—countries in which the disease is endemic, who are HIV-1 antibody positive on an initial enzyme-linked immunoassay screening test, and who have repeatedly indeterminate results on HIV-1 Western blot along with HIV-1 RNA viral loads at or below the limit of detection.[6, 7] This pattern of HIV testing can also be seen in patients who have a false-positive HIV-1 test.

Although most commercially available HIV screening tests can detect both HIV-1 and HIV-2, they do not distinguish between the two viruses. The Bio-Rad Laboratories Multispot HIV-1/HIV-2 test is the only antibody test that can distinguish between HIV-1 and HIV-2 that is approved by the Food and Drug

Administration (FDA) and should be used if HIV-2 is suspected. In some commercial and public health laboratories, HIV-2 supplemental tests, such as HIV-2 immunoblot or HIV-2-specific Western blot, are available. However, none of these tests has been FDA approved for diagnosis or clinical management of HIV-2. HIV-2 viral load assays available in the United States are not FDA approved and hence cannot be recommended for clinical use. All HIV-2 cases should be reported to the HIV surveillance program of the state or local health department, which can arrange for additional confirmatory testing for HIV-2 by the CDC.

HIV-2 has a longer asymptomatic phase than HIV-1, with a slower progression to AIDS. The most common mode of HIV-2 transmission is through heterosexual sex. HIV-2 is less infectious than HIV-1, with a 5-fold lower rate of sexual transmission and 20- to 30-fold lower rate of vertical transmission.[3, 8, 9] Several studies confirm that rates of mother-to-child transmission (MTCT) of HIV-2 are low with and without interventions (0%–4%), which may be a result of reduced plasma viral loads and less cervical viral shedding, compared with that seen in HIV-1-infected women.[10-13] HIV-2 also can be transmitted through breastfeeding. HIV-2 infection does not protect against HIV-1 and dual infection, which carries the same prognosis as HIV-1 monoinfection, can occur.

Few data exist on which to base treatment decisions or strategies for prevention of mother-to-child transmission (PMTCT) in patients infected with HIV-2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and enfuvirtide are not active against HIV-2 and should not be used for treatment or prophylaxis.[14, 15] HIV-2 has variable sensitivity to protease inhibitors (PIs), with lopinavir, saquinavir, and darunavir having the most activity against the virus.[16] The integrase inhibitors raltegravir and elvitegravir also appear to be effective against HIV-2.[3, 17, 18]

The care of HIV-2-infected pregnant women has been based on expert opinion. A regimen with two nucleoside reverse transcriptase inhibitors and a boosted PI currently is recommended for HIV-2-infected pregnant women who require treatment for their own health because they have significant clinical disease or CD4-cell counts <500 cells/mm^3.[19] Based on available data on safety in pregnancy, zidovudine/lamivudine plus lopinavir/ritonavir would be preferred. Tenofovir plus lamivudine or emtricitabine plus lopinavir/ritonavir can be considered as an alternative.[20, 21] NNRTIs should not be used because they are not active against HIV-2. All infants born to mothers infected with HIV-2 should receive the standard 6-week zidovudine prophylactic regimen.

For HIV-2-infected pregnant women with CD4-cell counts >500 cells/mm^3 and no significant clinical disease, who do not require treatment for their own health, some experts would use a boosted PI-based regimen for prophylaxis and stop the drugs postpartum. Other experts would consider zidovudine prophylaxis alone during pregnancy and intrapartum.[11] Because HIV-2 has a significantly lower risk of MTCT than does HIV-1, single-drug prophylaxis with zidovudine alone can be considered for PMTCT. All infants born to mothers infected with HIV-2 should receive the standard 6-week zidovudine prophylactic regimen.[21] The possible risks and benefits of antiretroviral (ARV) prophylaxis should be discussed with the mothers.

Pregnant women who have HIV-1/HIV-2 coinfection should be treated according to the guidelines for HIV-1-monoinfected patients, making sure that the ARV regimen chosen is also appropriate for HIV-2.

Other than the standard obstetrical indications, no data exist regarding the role of elective cesarean delivery in women who are infected with HIV-2. The risk to infants from breastfeeding is lower for HIV-2 than for HIV-1, but breastfeeding should be avoided in the United States and other resource-rich countries where safe infant formula is readily available.[11]

Infants born to HIV-2-infected mothers should be tested for HIV-2 infection with HIV-2-specific virologic assays at time points similar to those used for HIV-1 testing.[22] HIV-2 virologic assays are not commercially available, but the National Perinatal HIV Hotline (1-888-448-8765) can provide a list of sites that perform this testing.

Testing of infants at age 18 months (for example, with the Bio-Rad Laboratories Multispot HIV-1/HIV-2 test) also is recommended to confirm clearance of HIV-2 antibodies.[21]

References

1. De Cock KM, Brun-Vezinet F. Epidemiology of HIV-2 infection. *AIDS*. 1989;3(Suppl 1):S89-95. Available at http://www.ncbi.nlm.nih.gov/pubmed/2514761.
2. De Cock KM, Adjorlolo G, Ekpini E, et al. Epidemiology and transmission of HIV-2. Why there is no HIV-2 pandemic. *JAMA*. Nov 3 1993;270(17):2083-2086. Available at http://www.ncbi.nlm.nih.gov/pubmed/8147962.
3. Campbell-Yesufu OT, Gandhi RT. Update on human immunodeficiency virus (HIV)-2 infection. *Clin Infect Dis*. Mar 15 2011;52(6):780-787. Available at http://www.ncbi.nlm.nih.gov/pubmed/21367732.
4. Barin F, Cazein F, Lot F, et al. Prevalence of HIV-2 and HIV-1 Group O infections among new HIV diagnoses in France: 2003-2006. *AIDS* 2007 Nov 12;21 (17):2351-53. Available at http://www.ncbi.nlm.nih.gov/pubmed/18090288.
5. Centers for Disease Control and Prevention. HIV-2 Infection Surveillance--United States, 1987-2009. *MMWR Morb Mortal Wkly Rep*. Jul 29 2011;60(29):985-988. Available at http://www.ncbi.nlm.nih.gov/pubmed/21796096.
6. O'Brien TR, George JR, Epstein JS, Holmberg SD, Schochetman G. Testing for antibodies to human immunodeficiency virus type 2 in the United States. *MMWR Recomm Rep*. Jul 17 1992;41(RR-12):1-9. Available at http://www.ncbi.nlm.nih.gov/pubmed/1324395.
7. Torian LV, Eavey JJ, Punsalang AP, et al. HIV type 2 in New York City, 2000-2008. *Clin Infect Dis*. Dec 1 2010;51(11):1334-1342. Available at http://www.ncbi.nlm.nih.gov/pubmed/21039219.
8. Kanki PJ, Travers KU, S MB, et al. Slower heterosexual spread of HIV-2 than HIV-1. *Lancet*. Apr 16 1994;343(8903):943-946. Available at http://www.ncbi.nlm.nih.gov/pubmed/7909009.
9. Matheron S, Courpotin C, Simon F, et al. Vertical transmission of HIV-2. *Lancet*. May 5 1990;335(8697):1103-1104. Available at http://www.ncbi.nlm.nih.gov/pubmed/1970407.
10. O'Donovan D, Ariyoshi K, Milligan P, et al. Maternal plasma viral RNA levels determine marked differences in mother-to-child transmission rates of HIV-1 and HIV-2 in The Gambia. MRC/Gambia Government/University College London Medical School working group on mother-child transmission of HIV. *AIDS*. Mar 10 2000;14(4):441-448. Available at http://www.ncbi.nlm.nih.gov/pubmed/10770548.
11. Burgard M, Jasseron C, Matheron S, et al. Mother-to-child transmission of HIV-2 infection from 1986 to 2007 in the ANRS French Perinatal Cohort EPF-CO1. *Clin Infect Dis*. Oct 1 2010;51(7):833-843. Available at http://www.ncbi.nlm.nih.gov/pubmed/20804413.
12. Adjorlolo-Johnson G, De Cock KM, Ekpini E, et al. Prospective comparison of mother-to-child transmission of HIV-1 and HIV-2 in Abidjan, Ivory Coast. *JAMA*. Aug 10 1994;272(6):462-466. Available at http://www.ncbi.nlm.nih.gov/pubmed/8040982.
13. Andreasson PA, Dias F, Naucler A, Andersson S, Biberfeld G. A prospective study of vertical transmission of HIV-2 in Bissau, Guinea-Bissau. *AIDS*. Jul 1993;7(7):989-993. Available at http://www.ncbi.nlm.nih.gov/pubmed/8357558.
14. Tuaillon E, Gueudin M, Lemee V, et al. Phenotypic susceptibility to nonnucleoside inhibitors of virion-associated reverse transcriptase from different HIV types and groups. *J Acquir Immune Defic Syndr*. Dec 15 2004;37(5):1543-1549. Available at http://www.ncbi.nlm.nih.gov/pubmed/15577405.
15. Poveda E, Rodes B, Toro C, Soriano V. Are fusion inhibitors active against all HIV variants? *AIDS Res Hum Retroviruses*. Mar 2004;20(3):347-348. Available at http://www.ncbi.nlm.nih.gov/pubmed/15117459.
16. Desbois D, Roquebert B, Peytavin G, et al. In vitro phenotypic susceptibility of human immunodeficiency virus type 2 clinical isolates to protease inhibitors. *Antimicrob Agents Chemother*. Apr 2008;52(4):1545-1548. Available at http://www.ncbi.nlm.nih.gov/pubmed/18227188.

17. Roquebert B, Damond F, Collin G, et al. HIV-2 integrase gene polymorphism and phenotypic susceptibility of HIV-2 clinical isolates to the integrase inhibitors raltegravir and elvitegravir in vitro. *J Antimicrob Chemother*. Nov 2008;62(5):914-920. Available at http://www.ncbi.nlm.nih.gov/pubmed/18718922.

18. Bercoff DP, Triqueneaux P, Lambert C, et al. Polymorphisms of HIV-2 integrase and selection of resistance to raltegravir. *Retrovirology*. 2010;7:98. Available at http://www.ncbi.nlm.nih.gov/pubmed/21114823.

19. 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 June 19, 2012.

20. Gilleece Y, Chadwick DR, Breuer J, et al. British HIV Association guidelines for antiretroviral treatment of HIV-2-positive individuals 2010. *HIV Med*. Nov 2010;11(10):611-619. Available at http://www.ncbi.nlm.nih.gov/pubmed/20961377.

21. de Ruiter A, Mercey D, Anderson J, et al. British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. *HIV Med*. Aug 2008;9(7):452-502. Available at http://www.ncbi.nlm.nih.gov/pubmed/18840151.

22. Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PediatricGuidelines.pdf. Accessed June 19, 2012.