Guidelines for Use of HIV Combination Antiretroviral Therapy in the Perinatal Period

- Optimal prevention of perinatal HIV transmission includes administration of combination antiretroviral therapy (cART) to all HIV-infected women during pregnancy, regardless of CD4+ count and viral load (VL), and administration of zidovudine (ZDV, AZT, Retrovir) to all HIV-exposed infants. See "Follow-up Care for HIV Exposed Infants" for cART guidelines for high-risk infant exposures.
- Treatment goals of cART include an undetectable maternal VL.
- Initiation of maternal cART in the first trimester is preferred, but benefits to beginning cART exist throughout the prenatal period, including late in pregnancy.
- The known benefits and potential risks of cART use during pregnancy should be discussed with all HIV-positive women.
- The Antiretroviral Pregnancy Registry has reported no increase in birth defects among infants born to women receiving cART during pregnancy. Long term impact of in-utero exposure to cART is unknown.
- Encourage strict adherence to cART to prevent perinatal HIV transmission and drug resistance.

Initial Assessment and Ongoing Care

- Obtain an accurate history of prior cART use, adherence, tolerance, and resistance testing.
- Initial labs:

CD4+ count/%	HepBsAb	TB testing	LFTs
HIV VL	HepBcAb	Resistance test	Toxoplasmosis
HepBsAg	HepCAb	CBC	

- Additional labs may be indicated:
  - Testing for the HLA-B*5701 allele should be performed and a negative result documented before prescribing abacavir (ABC, Ziagen). Women should be educated on hypersensitivity signs/symptoms.
  - Test for HepAAb if HBV or HCV positive.
- Resistance testing should be performed on treatment naïve and experienced patients, and women entering pregnancy with detectable VL on cART, if VL >500 copies/ml.
- Monitor CD4+ count/% every 3 months. May reduce to every 6 months for women with consistently suppressed VL and reconstituted CD4+ count/%.
- Monitor cART effectiveness via HIV VL: VL at initial visit, 2-4 weeks after starting or changing cART, monthly until VL undetectable, every 3 months while undetectable, and at 34-36 weeks to assist with decision on mode of delivery.
- Assess need for pneumovax, seasonal flu vaccine, Tdap, TB testing, and HepB vaccine (if not immunized).
- Include case management and psychosocial support as needed.

Use of cART During Prenatal and Intrapartum Periods

First trimester of pregnancy, cART naive women:

- Start cART as soon as possible in the first trimester or delay until 12 weeks of pregnancy depending on CD4+ count, VL, maternal hyperemesis, and patient concerns about cART exposure.

First trimester of pregnancy, women currenty receiving cART therapy:

- Continue therapy if VL is optimally suppressed and side effects are minimal.

Women previously on cART or HIV prophylaxis, but not currently on cART:

- Choose regimen based on resistance testing and prior treatment history.

Second and third trimester of pregnancy, women currently receiving cART:

- Continue therapy if VL is optimally suppressed and side effects are minimal.
- Due to its ability to rapidly suppress VL, option to add raltegravir (RAL, Isentress) to cART regimen in the last trimester if high VL.

Intrapartum management :

- IV ZDV recommended if VL >1,000 copies/ml near labor. IV ZDV loading dose is 2 mg/kg over 1 hour, then 1 mg/kg/hour until delivery.
- Avoid invasive procedures (i.e., fetal scalp electrodes, forceps) if possible.
- There is no benefit of IV ZDV during labor if, 1) the patient is on an effective cART regimen during pregnancy, 2) VL <1,000 copies/ml consistently near delivery, and 3) there are no concerns about cART adherence.
- Continue cART regimen during L&D and permit oral doses.

For additional information, see "Recommendations for Use of Antiretroviral Drugs During Pregnancy" at http://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0.

Hepatitis B Virus (HBV)/Hepatitis C Virus (HCV) Co-infection

- Screen all pregnant women for HBV/HCV/HAV. If HepBsAg, HepBsAb, and HepBcAb negative, vaccinate for protection against HBV.
- For patients with chronic HBV (HepBsAg positive for >6 months), use a 3-drug regimen including a dual NRTI/NtRTI backbone of tenofovir (TDF, Viread) and lamivudine (3TC, Epivir) *or* emtricitabine (FTC, Emtriva).
- Women with chronic HBV and/or HCV infection who are negative for HAV should receive HAV vaccination.
- If cART is discontinued, monitor LFTs due to possible HBV flare.
- Interferon-alpha and pegylated interferon-alpha are not recommended, and ribavirin is contraindicated, during pregnancy.

Use with Caution

- There is a potential risk of neural tube defects with use of EFV early in pregnancy (first 5-6 weeks). May be initiated after 8 weeks of pregnancy when neural tube closure is complete. EFV is a preferred agent for treatment naïve women after 8 weeks of pregnancy.
- Unnecessary changes to cART regimens may be associated with loss of viral control. If pregnancy occurs while virally suppressed on EFV-containing cART regimen, EFV can be continued. Consider monitoring fetus with second trimester ultrasound.
- Use EFV with caution in non-pregnant women of childbearing potential to avoid use during first 8 weeks of unplanned pregnancy.
- Nevirapine (NVP, Viramune) should not be initiated in treatment naïve women with CD4+ counts >250. Monitor LFTs closely. Women who conceive on NVP may continue use regardless of CD4+ count if virally suppressed.
- If an NNRTI is stopped electively or after delivery, stop the NNRTI first and continue either dual NRTIs alone or with a PI for 7-30 days after stopping the NNRTI.
- Amniocentesis can be performed only if the patient is on an effective cART regimen with undetectable VL and is counseled about risks and benefits.

Scheduled Cesarean Section (C/S)

- VL at 34-36 weeks gestation determines preferred mode of delivery.
- Counsel women about the benefits of C/S to reduce vertical HIV transmission among patients with VL >1,000 copies/ml or unknown near delivery.
- Schedule C/S for HIV-related indications at 38 weeks gestation. Schedule C/S for other indications at 39 weeks.
- The benefit of C/S to prevent vertical HIV transmission is not clear after onset of labor or rupture of membranes.
- If VL >1,000 copies/ml near delivery, initiate IV ZDV 3-4 hours prior to C/S.
- Oral cART should be given on the day of delivery, regardless of C/S or vaginal delivery. No doses should be missed. (See "Use with Caution.")
- Laboring women with ZDV resistance should receive IV ZDV, if clinically indicated, as it will provide prophylaxis to the infant.
- For postpartum hemorrhage, avoid methergine with PIs, EFV, and etravirine (ETR, Intelence).

Developed by the Division of ID/HIV Medicine,
Drexel University College of Medicine and the Pennsylvania/MidAtlantic AIDS Education and
Training Center, Philadelphia Local Performance Site, Health Federation of Philadelphia. HRSA Grant No. H4AHA 00060. Updated October 2014.

Guidelines for Use of HIV Combination Antiretroviral Therapy in the Perinatal Period (cont.)

Postpartum Period

- Breastfeeding is not recommended in the US, where safe alternatives to breast milk are available.
- Counsel women against premastication of food for infants.
- Assess for barriers to optimal cART regimens for mother and infant. Challenges to maternal cART adherence are common immediately postpartum.
- Refer women to specialty HIV care providers for ongoing HIV treatment.
- Postpartum cART is generally recommended for all women, regardless of CD4+ count/%. Consider past cART use, resistance profile, adherence history, and patient preference when continuing/discontinuing regimens.

Follow-up Care for HIV Exposed Infants

The following should be performed by the delivering hospital in collaboration with a pediatric practice specializing in HIV:

- The delivering hospital should immediately notify the pediatric HIV practice about an infant HIV exposure.
- Initial and ongoing labs:
  - Baseline CBC (ZDV can cause anemia)
  - Optional HIV DNA PCR at birth
  - HIV DNA PCR at ages 14-21 days, 1-2 months, and 4-6 months
- Subsequent monitoring of hematologic status relies on the baseline lab values, prescribed medications, gestational age at birth, and clinical condition.
- Infant ZDV dosing: 4mg/kg/dose every 12 hours or 2 mg/kg/dose every 6 hours for 6 weeks. ZDV for 4 weeks may be considered if maternal VL was suppressed with consistent cART use during pregnancy.
- Preterm infants require dosing modifications; follow gestational-age appropriate dosing guidelines.
- If high risk exposure (i.e., mother diagnosed in labor, seroconverted in pregnancy, or with high VL), 3 doses of NVP are recommended, administered at birth, 48 hours after the first dose, and 96 hours after the second dose.
- Ensure that the mother understands and demonstrates correct administration of infant ZDV prior to discharge.
- Patients should not leave the delivering hospital without liquid ZDV and an appropriately-sized syringe (both often unavailable at local pharmacies).

HIV Testing and Care for Women at High-Risk

HIV Testing During the Perinatal Period

- HIV testing should be recommended for all women at the first prenatal visit, regardless of perceived risk.
- Repeat HIV testing should be recommended in the third trimester, preferably <36 weeks, if receiving health care in high-incidence jurisdictions, have signs/symptoms of acute HIV infection, or are personally considered at high-risk (as described below).
- Women are considered at elevated risk to acquire HIV if they are injection drug users, exchange sex for money or drugs, have had more than one sex partner during pregnancy, acquired a new STI during pregnancy, or have a known HIV-positive sex partner.
- If acute HIV infection is suspected at any time during pregnancy or breastfeeding, an antigen/antibody combination immunoassay ("4th generation test") or plasma HIV RNA test should be performed.
- If acute HIV is suspected during breastfeeding, counsel the woman to stop breastfeeding until test results are confirmed. Women may pump to preserve milk production until HIV infection is excluded.

HIV Testing in Labor and Delivery

- HIV tests are recommended for laboring women with no or limited prenatal care, who were not offered or declined testing in pregnancy, and without available third trimester HIV test results (if third trimester testing is indicated).
- Identifying HIV infection during labor may impact the clinical outcomes of the infant. HIV transmission occurs in 25% of HIV-exposed infant cases in the absence of recommended treatment, which decreases to 10% with only intrapartum and infant treatment. Transmission risk is <1% when all recommended maternal and infant treatment is provided.

Consenting, Counseling, and Giving Positive Results in Labor

- To assure confidentiality, tell family members and other visitors that examinations are performed privately.
- Convey that HIV testing is voluntary and confidential.
- Pennsylvania law states that providers can document verbal patient consent for HIV tests in the electronic or paper medical chart.
- Pre-test information (i.e., purpose, potential uses, limitations, meaning of results) must be provided for the purposes of informed consent.
- If HIV test results are preliminarily or confirmed positive, inform the woman of her status and counsel on the benefits of IV ZDV, as well as interventions that will reduce perinatal HIV transmission.
- If HIV testing results are preliminarily or confirmed positive, initiate the linkage to care protocol while the patient is still on L&D.

Resources for OB/GYNs and Women's Health Providers

National Resources

National Perinatal Hotline, UCSF: Clinical advice 24/7 on testing and care of HIV infected women and their infants, PH. 888-448-8765

Antiretroviral Pregnancy Registry: Register all HIV-positive pregnant women to track fetal risk of exposure to HIV medications. PH. 800-258-4263, Fax. 800-800-1052, http://www.apregistry.com

Philadelphia Resources

Perinatal Medical Case Management, ActionAIDS: Intensive case management services for HIV-positive pregnant/postpartum women receiving care in Philadelphia. Referral 24/7. PH. 215-981-0088, Fax. 215-243-2825

Philadelphia Local Performance Site of the PA/MidAtlantic AIDS Education and Training Center: Capacity building, resources, and on-site provider training on HIV-related topics, PH. 215-557-2101

Philadelphia's Pediatric HIV Specialty Practices

- **The Children's Hospital of Philadelphia**, Special Immunology, Family Clinic, 3550 Market Street, 4th floor, PH. 215-590-2549
- **St. Christopher's Hospital for Children**, Dorothy Mann Center for Pediatric and Adolescent HIV, Erie Avenue at Front Street, PH. 215-427-5284

Thank you to Erika Aaron, MSN, CRNP, Director of Women's Services, Drexel University College of Medicine, and Tina Penrose, RN, MSN, MPH, Project Coordinator, Pennsylvania/MidAtlantic AIDS Education and Training Center, Health Federation of Philadelphia, for their contributions to this guide. Questions? Contact the Pennsylvania/MidAtlantic AIDS Education and Training Center's Philadelphia local performance site at (215) 557-2101.

The HEALTH FEDERATION of Philadelphia

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PA/MidAtlantic AIDS Education and Training Center Headquarters, 412-624-1895, **www.pamaaetc.org**

For the most updated DHHS guidelines, see http://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0.
This document reflects guidelines published on 3/28/14.