A Handbook for the healthcare professional: guidelines and recommendations for the prevention of Perinatal HIV Transmission in Texas

Lend a helping hand

Texas Consortium for Perinatal HIV Prevention

Inside:

Recommendations for HIV Testing of Pregnant Women in Texas•
Guidelines for Care for HIV-infected Pregnant Women in Texas

"Dedicated to decreasing perinatal HIV transmission in Texas"

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Texas Consortium for Perinatal HIV Prevention

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Recommendations for HIV-Testing of Pregnant Women in Texas

Based on (i) The Centers for Disease Control and Prevention recommendations with additional modifications; MMWR September 22, 2006 / 55(RR14); 1-17; and (ii) Texas Health and Safety Code 81.090.

1. UNIVERSAL OPT-OUT SCREENING

1.1. All pregnant women in the State of Texas should be screened for HIV infection.

1.2. Screening should occur after a woman is notified that HIV screening is recommended for all pregnant patients and that she will receive an HIV test as part of the routine panel of prenatal tests unless she declines (opt-out screening).

1.3. HIV testing must be voluntary and free from coercion. No woman should be tested without her knowledge.

1.4. Prior to being tested, pregnant women should receive written information that includes an explanation of HIV infection, a description of interventions that can reduce HIV transmission from mother to infant, and the meanings of positive and negative test results. Women should be offered an opportunity to ask questions and to decline testing.

1.5. No separate signed informed consent shall be required for HIV testing. The verbal notification for the HIV test should be documented in the medical records.

1.6. If a patient declines an HIV test, this decision should be documented in the medical record.

2. TIMING OF HIV TESTING IN PREGNANCY

2.1. Initial Test: To promote informed and timely therapeutic decisions, health-care providers should test women for HIV at the very first health care visit, inpatient or outpatient. Women who decline the test early in prenatal care should be encouraged to be tested at a subsequent visit.

2.1.1. No separate signed informed consent shall be required for HIV testing. The verbal notification for the HIV test should be documented in the medical records.

2.2. A second HIV test during the third trimester, preferably at 32-36 weeks of gestation, should be performed on all pregnant women.

2.2.1. No separate signed informed consent shall be required for HIV testing. The verbal notification for the HIV test should be documented in the medical records.

2.3. All pregnant women who have positive confirmatory HIV test results shall be counseled immediately about the results, perinatal transmission risks, and methods of prevention. Health care providers should consult with specialists who are familiar with HIV treatment of pregnant women.

2.4. All labor and delivery facilities testing for HIV shall make HIV test results available within 6 hours of collection. Upon admission to labor and delivery facilities, the prior HIV test results shall be reviewed by the medical staff. Adequate documentation of prior HIV test results shall be conducted by review of copies of original medical records of prenatal clinic visits or by review of copies of original laboratory test results. Only written documentation of official medical records should be considered as evidence of HIV test results. Verbal information on the HIV test results provided by the patients shall not be acceptable.

2.5. Any woman without the result of an HIV test in the third trimester of pregnancy or with an undocumented HIV status during this pregnancy shall be tested for HIV at the time of labor, unless she declines (opt-out screening), with results available within 6 hours without waiting for a confirmatory test result.[1]

2.5.1.1. No separate signed informed consent shall be required for HIV testing. The verbal notification for the HIV test should be documented in the medical records.

2.6. Immediate initiation of appropriate antiretroviral prophylaxis should be recommended to women on the basis of a positive screening test result without waiting for the result of a confirmatory test, unless the patient has been previously identified to have a false-positive test or advised otherwise by an HIV specialist.

2.7. All women who have positive confirmatory HIV test results at delivery should be counseled immediately about the results and referred to specialists who can provide further HIV care.

3. POSTPARTUM TESTING OF MOTHERS

3.1. When a woman's HIV status is still unknown at the time of delivery, she should be tested immediately postpartum for HIV unless she declines (opt-out screening), with the intent to make the results available within 6 hours without waiting for a confirmatory test.

3.1.1. No separate signed informed consent shall be required for HIV testing. The verbal notification for the HIV test should be documented in the medical records.

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[1] This recommendation does not preclude institutions from continuing routine labor and delivery HIV testing in addition to the initial and third trimester testing. The results of such routine testing at delivery shall be made available within 6 hours without waiting for a confirmatory test.

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3.2. All women who have indeterminate HIV test results at delivery should have follow-up HIV tests at their post-partum visit within 1 month of delivery. If still indeterminate, repeat the tests at 3 and 6 months post-partum. If tests convert to confirmed positive, the women should be referred to specialists who can provide further HIV care and have their infants tested immediately for HIV infection by health care providers who are familiar with the testing and treatment protocol of infants.

4. INFANT TESTING

4.1. When the mother's HIV status is unknown postpartum, testing of the infant less 2 hours after the time of birth is recommended so antiretroviral prophylaxis can be offered to the HIV-exposed infant. The results should be available within 6 hours without waiting for a confirmatory test. The guardian should be informed that identifying HIV antibodies in the newborn indicates that the mother is infected.

4.1.1. No separate signed informed consent shall be required for HIV testing. The verbal assent of the parent/legal guardian for the HIV test should be documented in the medical records.

4.2. All infants of HIV confirmed positive mothers will be tested by virologic methods (HIV qualitative or quantitative viral genomic assay) soon after delivery (can be delayed until 2 weeks of age) and begin antiretroviral medication(s) within 12 hours after birth.

4.3. Infants of mothers with indeterminate HIV results may be tested as well by virologic methods and given antiretroviral medication(s) unless the mother is known to have previous false-positive results or advised otherwise by an HIV specialist.

4.4. All infants who are born to mothers with a confirmed positive HIV test should be evaluated for HIV infection by health care providers who are familiar with the testing and treatment protocol of infants.

5. CONFIRMATORY TESTING

5.1. Whenever possible, uncertainties regarding laboratory test results indicating HIV infection status should be resolved before final decisions are made regarding reproductive options, antiretroviral therapy, Cesarean delivery, or other interventions.

6. HIV INFECTION REPORTING

6.1. Any positive results for HIV screening or confirmatory testing of the mother at the first prenatal visit, during the third trimester, at delivery or after the birth of the child shall be reported to the local health authority. Any positive or negative test results from HIV testing of the newborn shall be reported to the local health authority.

Guidelines for Care for HIV-Infected Pregnant Women in Texas

This protocol is based on recommendations with modifications: *Public Health Service Task Force*- Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States (April 29, 2009) (http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf)

As an additional resource the National HIV/AIDS Clinician's Consultation Center has a National Perinatal HIV Consultation and Referral Service. This is a 24-hour Perinatal HIV Hotline providing free clinical consultation and advice on management of HIV in pregnant women, HIV testing in pregnancy, and care of HIV exposed infants. The phone number is 1-888-448-8765.

GUIDING PRINCIPLES

- **Select effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Contraceptive counseling is an essential component of care for HIV-infected women of reproductive age.**
- **For HIV-infected women who wish to become pregnant, offer counseling on perinatal HIV transmission and safe methods of conception.**
- **For HIV-infected women who are pregnant, provide access to specialized and coordinated HIV care that includes clinical assessment, combination HIV medication regimens and delivery options that are effective for maximal prevention of perinatal HIV transmission.**
- **For newborns of HIV-infected women, provide immediate access to appropriate HIV medications and HIV diagnostic and follow-up services.**
- **After delivery of the newborn, transition the HIV-infected mothers to appropriate long term HIV care.**

PRECONCEPTION COUNSELING

a) Select effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Providers should be aware of potential interactions of antiretroviral drugs with hormonal contraceptives that could lower contraceptive efficacy. Information on drug interactions can be found at (http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf)

b) Counsel on safe sexual practices that prevent HIV transmission to sexual partners and protect women from acquiring sexually transmitted diseases (STDs) and the potential to acquire more virulent or resistant HIV strains.

c) Choice of an antiretroviral regimen for treatment of HIV-infected women of childbearing age potentially needs to include consideration of effectiveness for treatment of her disease and the drug's potential for teratogenicity should pregnancy occur.

d) Counsel on eliminating alcohol, illicit drug use, and cigarette smoking.

e) For HIV-infected women who wish to become pregnant,

   i) A consultation with an HIV specialist (with expertise in preconception evaluation) is strongly recommended.

   ii) Educate and counsel women about risk factors for perinatal HIV transmission, strategies to reduce those risks, and potential effects of HIV or treatment on pregnancy course and outcomes.

   iii) Counsel on methods of reducing transmission to partner while attempting conception, e.g. ovulation predictor kits, home insemination.

   iv) Counsel on attaining a stable maximally suppressed viral load prior to conception for women who wish to become pregnant and benefits of delaying pregnancy until virologically suppressed and optimized immunological reconstitution

   v) Evaluate for appropriate prophylaxis for opportunistic infections and administration of medical immunizations (e.g. influenza, pneumococcal or Hepatitis B vaccines) as indicated.

   vi) Evaluate and control for therapy associated side effects that may adversely impact maternal-fetal health outcomes (e.g. hyperglycemia, anemia, hepatic toxicity).

   vii) Evaluate and adjust management of co-morbid conditions that may adversely impact maternal-fetal outcomes (e.g. HTN, hypercholesterolemia and therapies that may be teratogenic such as ACE-inhibitors, anti-HMG Co antagonist, etc)

ANTEPARTUM CARE

Medical care of the HIV-infected pregnant woman should involve coordinated services of obstetric and HIV specialists.

General Counseling

a) General counseling should include:

   i) Current knowledge regarding risk factors for perinatal transmission.

   ii) Cigarette smoking, illicit drug use, genital tract infections, and unprotected sexual intercourse with multiple partners during pregnancy have been associated with risk for perinatal HIV transmission.

iii) Use of condoms with sexual intercourse during pregnancy may also reduce risk of transmission to the partner.

iv) The Public Health Service Task Force recommends that HIV-infected women in the United States (including those receiving antiretroviral therapy) refrain from breastfeeding to avoid postnatal transmission of HIV to their infants through breast milk. (http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf). If a mother is HIV positive she has several infant feeding options: 1) banked donor milk (all banked milk is donated from screened mothers and pasteurized) or 2) commercial infant formula. If neither of these options is acceptable and if the patient is still considering breastfeeding, her physician should provide her counseling after conferring with an HIV expert.

v) The CDC is currently undergoing research to determine if HIV transmission is linked to the practice of premastication of food by the child's caregiver. (Three cases of HIV transmission have been identified to be possibly related to this practice.) Other micro-organisms that could be passed through prechewing include Hepatitis B Virus, Epstein Barr Virus, Herpes Virus 8, Group A Streptococci, Helicobacter Pylori, and Streptococcus Mutans**.** Until the risk of premastication and modifying factors (eg, periodontal disease) are better understood, it is recommended that health care providers routinely query children's caregivers and expecting parents who are infected with HIV or at risk of HIV infection about this feeding practice and direct them to safer, locally available, feeding options. http://www.ncbi.nlm.nih.gov/pubmed/19620190

Clinical Assessment

In addition to the standard antenatal assessments for all pregnant women, the initial evaluation of an HIV-infected pregnant woman should include an assessment of HIV disease status and recommendations regarding antiretroviral treatment or alteration of her current antiretroviral regimen.

a) The initial clinical assessment should include the following:

i) evaluation of the degree of existing immunodeficiency determined by past and current CD4 count;

ii) evaluation of the risk for disease progression and perinatal HIV transmission as determined by current plasma HIV RNA copy number;

iii) assessment of the need for prophylaxis against opportunistic infections such as *Pneumocystis jirovecii* pneumonia (PCP) or *Mycobacterium avium* complex (MAC) based on CD4 count;

iv) baseline evaluation with complete blood cell count, and renal and liver function testing;

v) investigation of hepatitis C infection (hepatitis C antibody);

vi) investigations of sexually transmitted infections, including syphilis, hepatitis B, gonorrhea, Chlamydia, as per routine obstetric practice;

vii) cervical cytology screening (pap smear);

viii) investigation of tuberculosis by tuberculin skin testing, unless performed in the previous year;

ix) history of prior and current antiretroviral therapy;

x) history of prior antiretroviral drug use for prevention of perinatal HIV transmission;

xi) results of prior and current HIV antiretroviral drug resistance studies;

xii) in general, if plasma HIV RNA is detectable, antiretroviral drug resistance studies should be performed before starting antiretroviral therapy or prophylaxis. However, if HIV is diagnosed late in pregnancy, therapy should be initiated while awaiting results of resistance testing;

xiii) assessment of supportive care needs.

Recommendations for Use of Antiretoviral Drugs during Pregnancy

The antiretroviral recommendations below are divided into sections according to antiretroviral treatment status at the time the woman presents for care and whether there are indications for therapy.

- **Recommendations for antiretroviral therapy during pregnancy must be individualized according to the specific antiretroviral history of the HIV-infected pregnant woman. Some women may be receiving antiretroviral therapy for their own health at the time they become pregnant, and present for obstetrical care on such therapy. Other HIV-infected women may not be receiving antiretroviral therapy at the time they present for obstetrical care. Some of these women will never have received antiretroviral drugs before, while other women may have previously received antiretroviral drugs, either for treatment that was stopped or for prophylaxis to prevent perinatal HIV transmission in prior pregnancies.**

- **Considerations for initiating therapy will differ for such women according to whether antiretroviral drugs are currently indicated for maternal health or solely for fetal protection**

- **The specific antiretroviral drugs used in pregnant women should conform, as much as possible, with those recommended by the Public Health Service Task Force (http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf). See Table 1.**

- **Although data are insufficient to support or refute the teratogenic risk of antiretroviral drugs when administered during the first 10 weeks of gestation, information to date does not support major teratogenic effects of the majority of antiretroviral drugs. However, certain drugs are of more concern than others (For example, efavirenz should be avoided during the first trimester of pregnancy).**

Clinical Scenario Summary Recommendations for Antiretroviral Drug Use in Pregnant Women

HIV-infected pregnant woman who is antiretroviral naïve

a) HIV antiretroviral drug resistance testing is recommended prior to the initiation of therapy, and if suboptimal viral suppression after initiation of highly active antitretroviral therapy (HAART).

b) For women who are receiving antiretroviral drugs solely for the prevention of perinatal transmission, consider delaying HAART initiation until after first trimester is completed. For women who require immediate initiation of therapy for their own health as per guidelines for non-pregnant adults (eg. advanced HIV infection), treatment should be initiated as soon as possible, including in the first trimester.

c) Initiate three-drug combination HAART regimen. The standard HAART regimen includes two reverse transcriptase inhibitors (NRTIs) combined with one protease inhibitor (PI) or one non-nucleoside reverse transcriptase inhibitor (NNRTI).

   i) The preferred HAART regimen for pregnant women is (see Table 1 for doses):

      (1) Two NRTIs: zidovudine (ZDV) + lamivudine (3TC)

      (2) Add to above one of the agents below:

         a. A protease inhibitor: lopinavir/ritonavir (LPV/RTV) or nelfinavir OR

         b. A non-nucleoside reverse transcriptase inhibitor (NNRTI): nevirapine (NVP) only for women with CD4 count ≤250 cells/mm^3. NVP should only be used as a component of therapy in women with CD4 counts >250 cells/mm^3 if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity.

   ii) The above regimen can be modified based on the results of antiretroviral resistance test results.

   iii) Avoid use of efavirenz (EFV) or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI).

   iv) Use of ZDV as a component of the antiretroviral regimen is recommended when feasible.

d) Continue HAART regimen during intrapartum period (ZDV given as continuous infusion as soon as labor begins while other antiretroviral agents are continued orally) and postpartum.

e) Scheduled Cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.

f) **Infant**: ZDV for 6 weeks started within 6 to 12 hours after birth.

HIV-infected woman who is receiving HAART and becomes pregnant

a) Continue current HAART regimen (at least a three-drug combination) if successfully suppressing viremia; except avoid use of efavirenz (EFV) or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI).

b) HIV antiretroviral drug resistance testing is recommended if the woman has detectable viremia on therapy.

c) In general, if woman requires treatment, antiretroviral drugs should not be stopped during the 1st trimester.

d) Continue HAART regimen during intrapartum period (ZDV given as continuous infusion during labor while other antiretroviral agents are continued orally) and postpartum.

e) Scheduled Cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.

f) **Infant**: Zidovudine (ZDV) for 6 weeks started within 6 to 12 hours after birth.

HIV-infected pregnant woman who is antiretroviral experienced but not currently receiving antiretroviral drugs

a) Obtain full antiretroviral treatment history and evaluate need for immediate antiretroviral treatment for own health (eg. advanced HIV infection).

b) Perform HIV antiretroviral drug resistance testing prior to initiating repeat antiretroviral prophylaxis or therapy, and if suboptimal viral suppression after initiation of HAART.

c) Initiate HAART, with regimen chosen based on resistance testing and prior therapy history.

d) Avoid use of efavirenz (EFV) or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI).

e) Use of zidovudine (ZDV) as a component of the antiretroviral regimen is recommended when feasible.

f) Nevirapine (NVP) should only be used as a component of therapy in women with CD4 counts >250 cells/mm3 if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity.

g) Continue HAART regimen during intrapartum period (ZDV given as continuous infusion during labor while other antiretroviral agents are continued orally).

h) Evaluate need for continued therapy postpartum; discontinue HAART unless has indications for continued therapy. If regimen includes drug with long half-life like NNRTI, consider stopping NRTIs 7 days after stopping NNRTI. (Limited data exist on this.).

i) Scheduled Cesarean delivery at 38 weeks gestation if plasma HIV RNA remains >1,000 copies/mL near the time of delivery.

j) **Infant:** ZDV for 6 weeks started within 6 to 12 hours after birth.

HIV-infected woman who has received no antiretroviral therapy prior to labor (Table 3)

Begin therapy with one of the following choices:

Choice #1
Woman*:* ZDV given as continuous infusion during labor.
Infant: ZDV for 6 weeks started within 6 to 12 hours after birth.

Choice #2
Combination ZDV + Single-Dose NVP:
Woman: ZDV given as continuous infusion during labor, plus single-dose NVP at onset of labor. Consideration should be given to adding 3TC during labor and maternal ZDV/3TC for 7 days postpartum, which may reduce development of NVP resistance.
Infant: Single-dose NVP plus ZDV for 6 weeks.

Choice #3
Woman*:* ZDV given as continuous infusion during labor.
Infant: Some clinicians may choose to use ZDV in combination with additional drugs in the infant, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended.

Note: Evaluate need for initiation of maternal therapy postpartum.

Infant born to HIV-infected woman who has received no antiretroviral therapy prior to or during labor

a) ZDV given for 6 weeks to the infant, started as soon as possible after birth.

b) ***OR,*** some clinicians may choose to use ZDV in combination with additional drugs, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended.

c) Evaluate need for initiation of maternal therapy postpartum.

Recommendations regarding Mode of Delivery to Reduce Perinatal HIV Transmission

a) Vaginal delivery should be allowed in HIV-infected women on HAART with an undetectable HIV RNA level at 36 weeks gestation. The woman should be counseled that her risk of perinatal transmission of HIV with a persistently undetectable HIV RNA level is low, probably 2% or less, even with vaginal delivery. There is currently no information to evaluate whether performing a scheduled Cesarean section will lower her risk further.

b) Cesarean section delivery should be offered to:
   i) HIV-infected women presenting in late pregnancy (after about 36 weeks gestation), known to be HIV-infected but not receiving antiretroviral therapy, and who have HIV RNA level and CD4 count pending but unlikely to be available before delivery. **OR**
   ii) HIV-infected women who initiated prenatal care early in the third trimester, are receiving HAART, and have an initial virologic response, but have HIV RNA levels that remain substantially more than 1,000 copies/mL at 36 weeks gestation.

c) If Cesarean section is chosen:
   i) The woman should be counseled that scheduled Cesarean section is likely to reduce the risk of transmission to her infant. She should also be informed of the increased risks to her from Cesarean section, including increased rates of postoperative infection, anesthesia risks, and other surgical risks.
   ii) The procedure should be scheduled at 38 weeks gestation based on the best available clinical information.
   iii) When scheduled Cesarean section is performed, the woman should receive continuous intravenous ZDV infusion beginning 3 hours before surgery and her infant should receive 6 weeks of ZDV therapy after birth.
   iv) Use of prophylactic antibiotics at the time of Cesarean delivery is generally recommended.

d) For HIV-infected women who have elected scheduled Cesarean section but present in early labor or shortly after rupture of membranes, intravenous ZDV should be started immediately since the woman is in labor or has ruptured membranes.
   i) If labor is progressing rapidly, the woman may deliver vaginally.
   ii) If cervical dilatation is minimal and a long period of labor is anticipated, some clinicians may choose to administer the loading dose of intravenous ZDV and proceed with Cesarean section to minimize the duration of membrane rupture and avoid vaginal delivery. Others might begin pitocin augmentation to enhance contractions and potentially expedite delivery.
   iii) If the woman is allowed to labor, artificial rupture of membranes and scalp electrodes, and operative delivery should be avoided if possible.

ACCESS TO HIV MEDICATIONS

a) HIV-infected pregnant women and their newborn infants should be managed by clinicians knowledgeable about access to medications.
   i) Clinicians must familiarize themselves with the local community HIV service organizations that can help identify resources for medications. The local health departments can provide information on the HIV service organizations.

ii) All uninsured pregnant women should be screened for Medicaid/CHIP eligibility at the very first encounter.
iii) For uninsured patients, clinicians must assist the pregnant women for enrollment in the Texas HIV Medication Program. (http://www.dshs.state.tx.us/hivstd/meds/document.shtm)

b) Clinicians and hospitals must ensure that access to the HIV medications for pregnant women and infants is available on urgent basis if necessary.

c) At a minimum, all hospitals that provide labor and delivery services must stock IV zidovudine (ZDV) for the mother and oral liquid forms of zidovudine (ZDV) for infants. Hospitals should also consider stocking the other commonly used HIV medications; these include:
   i) Tablet/capsule form for adults: zidovudine, lamivudine, nelfinavir, lopinavir/ritonavir, nevirapine
   ii) Oral liquid form for infants: lamivudine, Nevirapine

d) All hospitals that provide labor and delivery services must provide all newborn infants of HIV-positive mothers a full six-week course of oral zidovudine and detailed instructions on administration at the time of discharge.
   i) Due to the low cost of liquid zidovudine and the difficulty of obtaining liquid zidovudine from outpatient pharmacies, hospitals should provide the full six-week supply of zidovudine from the same bottle that is used for inpatient dispensing (the left over volume is often discarded).

POSTNATAL CARE

a) Any HIV infected woman who had a pregnancy resolution should be referred to an HIV specialist facility for continuity of her HIV and primary care, regardless of the status of the infant or if the pregnancy did not result in a live birth
   i) Determination of continuation of antiretroviral therapy should be done at their first follow up appointment based on current U.S. Department of Health and Human Services (DHHS) guidelines for the management of antiretrovirals in adolescents and adults http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf
   ii) Adequate amounts of ARV should be given and doses reviewed

b) Any HIV infected woman who had a pregnancy resolution should be counseled and offered additional contraceptive options upon discharge

c) Any newly diagnosed HIV infected woman who had a pregnancy resolution should be counseled on prevention of HIV transmission, importance of continuity of care and future reproductive decisions.

Table 1. Recommended HIV Medications in HIV-Infected Pregnant Women

Antiretroviral Drug	Dosage in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
NRTIs/ NtRTIs			
Recommended agents			
Zidovudine*		No evidence of human teratogenicity. Well-tolerated, short-term safety demonstrated for mother and infant.	Preferred NRTI for use in combination antiretroviral regimens in pregnancy based on efficacy studies and extensive experience; should be included in regimen unless significant toxicity or stavudine use.
Lamivudine*		No evidence of human teratogenicity. Well-tolerated, short-term safety demonstrated for mother and infant.	Because of extensive experience with lamvudine in pregnancy in combination wth zidovudine, lamvudine plus zidovudine is the recommended dual NRTI backbone for pregnant women.
Alternate agents			
Didanosine		Cases of lactic acidosis, some fatal, have been reported in pregnant women receiving didanosine and stavudine together.	Alternate NRTI for dual nucleoside backbone of combination regimens. Didanosine should be used with stavudine only if no other alternatives are available.
Emtricitabine†		No studies in human pregnancy.	Alternate NRTI for dual nucleoside backbone of combination regimens.
Stavudine		No evidence of human teratogenicity. Cases of lactic acidosis, some fatal, have been reported n pregnant women receiving didanosine and stavudine together.	Alternate NRTI for dual nucleoside backbone of combination regimens. Stavudine should be used with didanosine only if no other alternatives are available. Do not use with zidovudine due to potential for antagonism.
Abacavir*		Hypersensitivity reactions occur in ~5%–8% of nonpregnant persons; a much smaller percentage are fatal and are usually associated with rechallenge. Rate in pregnancy unknown. Patient should be educated regarding symptoms of hypersensitivity reaction.	Alternate NRTI for dual nucleoside backbone of combination regimens.

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Table 1. Recommended HIV Medications in HIV-Infected Pregnant Women

Antiretroviral Drug	Dosage in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
Insufficient data to recommend use			
Tenofovir†		Studies in monkeys show decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy. Clinical studies in humans (particularly children) show bone demineralization with chronic use; clinical significance unknown. Significant placental passage in humans (cord: maternal blood ratio ~1.0).	Because of lack of data on use in human pregnancy and concern regarding potential fetal bone effects, tenofovir should be used as a component of a maternal combination regimen only after careful consideration of alternatives.
Not recommended			
Zalcitabine *(no longer available in the United States)*	No studies in human pregnancy.	Rodent studies indicate potential for teratogenicity and developmental toxicity.	Given lack of data and concerns regarding teratogenicity in animals, not recommended for use in human pregnancy unless alternatives are not available.
NNRTIs			NNRTIs are recommended for use in combination regimens with 2 NRTI drugs.
Recommended agents			
Nevirapine		No evidence of human teratogenicty. Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 counts >250/mm3 when first initiating therapy; unclear if pregnancy increases risk.	Nevirapine should be initated in pregnant women with CD4 counts >250 cells/mm3 only if benefit clearly outweighs risk, due to the increased risk of potentially life-threatening hepatotoxicity in women with high CD4 counts. Women who enter pregnancy on nevriapine regimens and are tolerating them well may continue therapy, regardless of CD4 count.
Not recommended			
Efavirenz† (FDA Pregnancy Class D)	No studies in human pregnancy.	Significant malformations (anencephaly, anophthalmia, cleft palate) were observed in 3 (15%) of 20 infants born to cynomolgus monkeys receiving efavirenz during the first trimester at a dose giving plasma levels comparable to systemic	Use of efavirenz should be avoided in the first trimester, and women of childbearing potential must be counseled regarding risks and avoidance of pregnancy. Because of the known failure rates of contraception, alternate regimens should be strongly considered in women of child-bearing potential. Use after the second trimester of pregnancy can be considered if other alternatives are not available and if adequate contraception can be assured postpartum.

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Table 1. Recommended HIV Medications in HIV-Infected Pregnant Women

Antiretroviral Drug	Dosage in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
		human therapeutic exposure; there are 3 case reports of neural tube defects in humans after first trimester exposure; relative risk unclear.	
Delavirdine	No pharmacokinetic studies in human pregnancy.	Rodent studies indicate potential for carcinogenicity and teratogenicity.	Given lack of data and concerns regarding teratogenicity in animals, not recommended for use in human pregnancy unless alternatives are not available.
Protease inhibitors			PIs are recommended for use in combination regimens with 2 NRTI drugs.
Recommended agents			
Lopinavir/ ritonavir		No evidence of human teratogenicity. Well-tolerated, short-term safety demonstrated in Phase I/II studies.	The capsule formulation is no longer available. Pharmacokinetc studies of the new tablet formulation are underway, but there are currently insufficient data to make a definitive recommendation regarding dosing in pregnancy. Some experts would administer standard dosing (2 tablets twice daily) throughout pregnancy and monitor virologic response and lopinavir drug levels, if available. Other experts, extrapolating from the capsule formulation pharmacokinetic data, would increase the dose of the tablet formulation during the third trimester (from 2 tablets to 3 tablets twice daily), returning to standard dosing postpartum. Once daily lopinavir/ritonavir dosing is not recommended during pregnancy because there are no data to address whether drug levels are adequate with such administration.
Alternate agents			
Indinavir (combined with low dose ritonavir boosting)		Theoretical concern re: increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in the neonate, but minimal placental passage. Use of unboosted indinavir during pregnancy is not recommended.	Alternate PI to consider if unable to use lopinavir/ritonavir, but would need to give indinavir as ritonavir-boosted regimen. Optimal dosing for the combination of indinavir/ritonavir in pregnancy is unknown.
Nelfinavir		No evidence of human teratogenicity. Well-tolerated, short-term safety demonstrated for mother	Given pharmacokinetic data and extensive experience with use in pregnancy, nelfinavir is an alternative PI for combination regimens in pregnant women receiving HAART only for perinatal

Table 1. Recommended HIV Medications in HIV-Infected Pregnant Women

Antiretroviral Drug	Dosage in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
		and infant.	prophylaxis. In clinical trials of initial therapy in non-pregnant adults, nelfinavir-based regimens had a lower rate of viral response compared to lopinavir-ritonavir or efavirenz-based regimens, but similar viral response to atazanavir or nevirapine-based regimens.
Ritonavir		Limited experience at full dose in human pregnancy; has been used as low-dose ritonavir boosting with other PIs.	Given low levels in pregnant women when used alone, recommended for use in combination with second PI as low-dose ritonavir "boost" to increase levels of second PI.
Saquinavir-hard gel capsule [HGC] (Invirase□)/ ritonavir		Well-tolerated, short-term safety demonstrated for mother and infant for both saquinavir-SGC and -HGC in combination with low-dose ritonavir.	Saquinavir-SGC is no longer available. There are only limited pharmacokinetic data on saquinavir-HGC and the new tablet formulation in pregnancy. Ritonavir-boosted saquinavir-HGC or saquinavir tablets are alternative PIs for combination regimens in pregnancy, and are alternative initial antiretroviral recommendations for non-pregnant adults.
Insufficient data to recommend use			
Amprenavir *(no longer available in the U.S.)*		Oral solution contraindicated in pregnant women because of high levels of propylene glycol, which may not be adequately metabolized during pregnancy.	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use of capsules during pregnancy.
Atazanavir		Theoretical concern re: increased indirect bilirubin levels, which may exacerbate physiologic hyperbilirubinemia in the neonate, although transplacental passage is very low and likely to be variable (10%).	Safety and pharmacokinetics in pregnancy data are insufficient to recommend use during pregnancy.

Table 2	Intrapartum Maternal and Neonatal Zidovudine Dosing for Prevention of Mother to Child HIV Transmission	
Maternal Intrapartum		
Drug	**Dosing**	**Duration**
ZDV	2 mg per kg body weight intravenously over 1 hour, followed by continuous infusion of 1 mg per kg body weight per hour	Onset of labor until delivery of infant; or 3 hours prior to elective Cesarean until delivery
Neonatal		
Drug	**Dosing**	**Duration**
ZDV (term [≥35 weeks] infant)	2 mg per kg body weight per dose given orally (or 1.5 mg per kg body weight per dose given intravenously) started as close to birth as possible (by 6-12 hours of delivery), then every 6 hours*	Birth to 6 weeks
ZDV (<35 weeks but >30 weeks)	2 mg per kg body weight per dose given orally (or 1.5 mg per kg body weight per dose given intravenously) every 12 hours, advanced to every 8 hours at 2 weeks of age	Birth to 6 weeks
ZDV (<30 weeks)	2 mg per kg body weight per dose given orally (or 1.5 mg/kg/dose given intravenously) every 12 hours, advanced to every 8 hours at 4 weeks of age	Birth to 6 weeks

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Table 3 Intrapartum Maternal and Neonatal Dosing for Additional Antiretroviral Drugs to be Considered Only in Selected Circumstances

Maternal Intrapartum/Postpartum		
Drug	**Dosing**	**Duration**
NVP (as single dose intrapartum)*	200 mg given orally as single dose	Given once at onset of labor
ZDV + 3TC (given with single dose NVP as "tail" to reduce NVP resistance	ZDV: IV intrapartum as per Table 2, then after delivery 300 mg orally twice daily 3TC: 150 mg orally twice daily starting at labor onset	Through 1 week postpartum

Neonatal		
Drug	**Dosing**	**Duration**
NVP (as single dose)**	2 mg per kg body weight given orally as single dose	Single dose between birth and 72 hours of age. If maternal dose is given $\leq$ 2 hours before delivery, infant dose should be administered as soon as possible following birth.
ZDV + 3TC (given with single dose NVP as "tail" to reduce NVP resistance)	ZDV: neonatal dosing as per Table 2 3TC: 2 mg per kg body weight given orally twice daily	ZDV: Birth to 6 weeks 3TC: Birth to 1 week

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ADDITIONAL COPIES/INFORMATION

To print additional copies of this document please visit the following website: http://aidseducation.org/products.html or go directly to the document at http://www.aidseducation.org/documents/PerinatalHIVGuidelines.pdf

The Texas Consortium for Perinatal HIV Prevention will adjust these guidelines and recommendations as strategies to prevent perinatal HIV continue to evolve. Please refer to the most recent version of this document at http://www.aidseducation.org/documents/PerinatalHIVGuidelines.pdf

For further information you may also refer to the AIDS*info* Web site (available at http://www.aidsinfo.nih.gov). The National Perinatal HIV Consultation and Referral Service at 888-448-8765 is also available to provide 24-hour clinical consultation and referral services.