

Important Information Regarding the Treatment of HIV-Positive Women December 2007

In September 2007, the Food and Drug Administration (FDA) and Pfizer Pharmaceuticals issued a joint statement recommending the discontinuation of Nelfinavir (Viracept) in pregnant patients until further notice due to the presence of a contaminant (ethylmethanesulfonate), which may be a potential teratogen. Therefore, the information in Improving the Odds regarding the use of Nelfinavir is no longer accurate.

For the full FDA explanation, please go to: <http://www.fda.gov/cder/drug/infopage/nelfinavir/default.htm>

For the most up-to-date (November 2007) Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States, please go to: <http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf>.

Addendum to Improving the Odds October 2005

On the inside cover of Improving the Odds, under the “Recommended Timing and Dosing of ZDV”, fourth point letter b, it states: “oral nevirapine (Viramune) can be used for the mother at the onset of labor and for the newborn 48-72 hours after birth”. Since the time Improving the Odds was written and printed, information on nevirapine (NVP) resistance (NVPR) after the administration of a single dose of nevirapine (SD-NVP) has emerged.

In the HIVNET 012 study, NVPR was detected in 25% of women and in 46% of infants 6-8 weeks after delivery. Emergence of NVPR after the administration of SD-NVP was subsequently observed in other studies. Results of a recent study suggest that women with prior exposure to SD-NVP may have a reduced virologic response to treatment regimens that contain nonnucleoside reverse-transcriptase inhibitors (NNRTI). It is not known whether prior exposure to SD-NVP reduces the efficacy of treatment regimens that contain NVP in HIV-1 infected children or the efficacy of SD-NVP for prevention of mother-to-child transmission in subsequent pregnancies. NVP resistant virus in women receiving SD-NVP could also potentially be transmitted to infants by breast feeding.

Few studies have evaluated the persistence of NVPR after the administration of SD-NVP. In the HIVNET 012 study, samples obtained 12-24 months after the administration of SD-NVP were available for 11 women and 6 infants who had NVPR at 6-8 weeks. After the administration of SD-NVP mutations were detected in those samples. In the HIVNET 023 trial, variants with NVPR mutations could not be detected in almost all women by 6 months postpartum. However, in South African cohort, 55(35%) of 155 women who had NVPR at 7 weeks postpartum still had detectable NVPR at 6 months postpartum.

In view of resistance development and persistence of the resistance pattern, SD NVP should not be used in HIV infected pregnant woman without consultation with an HIV medicine specialist.

The Michigan Department of Community Health (MDCH) recommends that, when a decision to deliver is made, maternal intrapartum intravenous Zidovudine (ZDV) start within one hour: initial dose of 2 mg/kg of body weight, followed by a continuous infusion of 1 mg/kg body weight/hour until the cord is clamped. (Point 4 under “Recommended Timing and Dosing of ZDV”)

MDCH recommends consultation with one of the experts listed in Improving the Odds for all high-risk scenarios when timely decisions about mode of delivery and antiretroviral choice, including SD-NVP, are crucial in the prevention of mother-to-child transmission.

For the most updated HIV/AIDS treatment information, visit www.aidsinfo.nih.gov or call the National Perinatal HIV Consultation and Referral Service at: 1-888-448-8765.

Reducing Perinatal HIV Transmission

Improving the Odds

Report of the Recommendations of the Maternal Child Health Advisory Committee

Perinatal HIV Prevention Working Group

2005

Moving Toward the Elimination of Perinatal HIV Transmission

All patients to be tested for HIV antibodies should be provided with pre and post test counseling in compliance with Michigan State HIV Mandatory Counseling and Informed Consent Law (MCL 333.5133: Public Act 488 of 1988, as amended by Act 200 of 1994 and Act 420 of 1994). Also note that HIV positive tests must be reported to MDCH or a local health department within seven days of obtaining a confirmatory positive test result, using form CDC 50.42A for adults or CDC form 50.42B for HIV perinatally exposed infants or a HIV positive child, in compliance with HIV Reporting Requirements (MCL 333.5114; Public Act 489 of 1988).

Michigan Public Health Code 333.5123-Prenatal HIV Counseling and Testing

The Prenatal Testing Requirement requires health care providers to test pregnant women for HIV or an antibody to HIV, hepatitis B, and sexually transmitted diseases at the time of a pregnant women's initial exam. The code also requires testing at the time of delivery if there are no test results or they are unavailable or in the immediate postpartum period if there is no record of test results, nor if there is a record of the woman's refusal to test. HIV testing must be provided unless the woman refuses consent or the health care provider determines the test medically inadvisable. The Michigan Department of Community Health also recommends retesting in the third trimester of pregnancy, prior to 36 weeks gestation.

- â All women's health care providers should routinely offer and provide HIV testing to all pregnant women and all women considering pregnancy.
- â All obstetricians, midwives, and other obstetrical providers should routinely discuss the risk of mother to child HIV transmission.

Documentation of Maternal HIV Status and Maternal HIV Therapies

The health care provider is required by Michigan law to record the client's test results and date of testing in her medical record. If testing is refused, this must be documented. If the health care provider did not order testing, an explanation of why the tests were not ordered must be documented.

- â During admission for labor and delivery, routine history taking should include ascertainment of HIV serostatus. If the woman's serostatus is unknown, she must be offered HIV testing, as stated above or rapid testing.
- â For women known to be HIV positive a history of Zidovudine and other antiretroviral medications used during pregnancy should be obtained.

Recommended Timing and Dosing of ZDV:

- â Maternal Therapy: Oral Administration of 100 mg ZDV five times daily, 200 mg three times daily, or 300 mg twice daily initiated at 14-34 weeks gestation and continued throughout the pregnancy.
- â Intrapartum: Intravenous administration of ZDV in one-hour initial dose of 2 mg/kg body weight, followed by a continuous infusion of 1 mg/kg body weight/hour until the cord is clamped.^{1,2,3,4}
- â Elective Caesarean section prior to the onset of labor should be considered for women on antiretroviral therapy who have a plasma HIV RNA level > 1,000 copies/mL at 36 weeks gestation, and women who present at 36 weeks gestation or later without prior antiretroviral therapy. For patients undergoing induction of labor, intravenous therapy should begin at the time induction of labor begins. For elective Cesarean section, intravenous therapy should begin 3 hours before the time of surgery.

- â For women in labor who have not received antiretroviral therapy during pregnancy, four regimens are available for consideration: (a) Intrapartum IV ZDV with oral ZDV for the newborn, as in the second and third components of the ACTG076 regimen; (b) oral nevirapine (Viramune) 200mg for the mother at the onset of labor, and 2mg/kg of oral nevirapine to the newborn within 48-72 hours of birth; (c) combined ZDV and lamivudine (Epivir) [maternal treatment during labor ZDV 300 mg po q3h with lamivudine 150 mg po q12h; infant treatment ZDV 4 mg/kg q 12h and lamivudine 2 mg/kg po q 12h, both for 7 days]; or (d) the combination of intrapartum and postpartum ZDV per the 076 protocol (as in regimen a) with oral nevirapine (as in regimen b).
- â Newborn Therapy: ZDV syrup at 2 mg/kg body weight/dose every six hours for the first six weeks of life, beginning at to 8-12 hours after birth.⁵

¹ If delivery is anticipated in less than 1/2 hour from the time of arrival, a bolus infusion of ZDV can be given. The drug must be diluted prior to administration; the maximum concentration that can be given is 4 mg/ml.

² ZDV is compatible with the following IV fluids: Normal Saline, D5 Normal Saline, Lactated Ringers, and D5 Lactated ringers.

³ The infusion can be piggy backed into the main IV line consult your pharmacy concerning compatibility with other medications.

⁴ A continuous IV infusion should result in maximum fetal/newborn drug levels.

Medical Reference Section

HIV/AIDS Treatment Information Services, PHS 1-800-HIV-0440 or <http://www.aidsinfo.nih.gov>

Perinatal Hotline 1-888-448-8765
 National Perinatal HIV Consultation and Referral Service
 24 hours a day/7 days a week

Warmline 1-800-933-3413
 National HIV Telephone Consultation Service
 Monday-Friday 8am-8pm EST
 Voicemail 24 hours a day/7 days a week

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Arthur James, MD, Borgess Medical Center (Kalamazoo)	269-226-7000
Theodore Jones, MD, WSU/DMC (Detroit)	313-745-4380*
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	313-745-0203 pager 2789#
Laura Zuidema, MD, West Michigan Perinatal Center (Grand Rapids)	616-391-3681

**Daytime clinic number and night/weekend answering service number*

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Jonathan Cohn, MD, WSU/DMC (Detroit)	313-745-9035*
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WELCOME

Welcome to the second edition of *Improving the Odds*. The first edition was developed between 1996 and 1998, by a sixty-member Michigan Department of Community Health (MDCH) advisory committee representing organizations serving women, children and infants. Consumers were also involved in the development of *Improving the Odds*. Several documents were used including the Centers for Disease Control and Prevention Recommendations for Universal Counseling and Voluntary Testing for HIV of Pregnant Women and the Clinical Guidelines for the Use of Zidovudine Therapy in Pregnancy to Reduce Perinatal Transmission of HIV, as developed by the New York State Department of Health AIDS Institute.

Since the first edition was released in 1998, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Public Health Service (PHS), and the American College of Obstetricians and Gynecologists (ACOG) have released medical guidelines, studies, and recommendations that can greatly improve the opportunity of further reducing mother to child (perinatal) HIV

transmission. Unless otherwise noted, all the information used to update the second edition of Improving the Odds included: The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, June 16, 2003, the Revised Recommendations for HIV Screening of Pregnant Women November 9, 2001, and the Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents, July 14, 2003.

The Michigan Department of Community Health is proud to release this updated edition of Improving the Odds to assist health care providers in providing HIV counseling and testing, care for and medically manage HIV pregnant women and their HIV exposed children.

PURPOSE

Improving the Odds offers health care providers current information on the reduction of perinatal HIV transmission. This guide reviews the United States Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, June 16, 2003. Improving the Odds also reviews the Michigan Department of Community Health, Public Health Code 333.5123, which requires all pregnant women to be offered HIV testing; and the United States Public Health Service Recommendations for HIV Counseling and Voluntary Testing for Pregnant Women.

Due to the rapid development of new therapies for treatment of HIV, this guide is not intended to represent the specifics of therapy in women infected with HIV. Women's health care providers caring for a pregnant woman with HIV should seek consultation from a clinician that has expertise in HIV and to work closely with the woman herself when making medical management decisions. For the most up-to-date clinical guidelines for prevention and treatment, please refer to <http://www.aidsinfo.nih.gov>. Perinatal HIV consultation and referral is available from the National Perinatal Hotline at 1-888-448-8765 24 hours a day, seven days a week. HIV clinical and drug information can also be obtained from the National HIV/AIDS Clinicians Consultation center Warmline at 1-800-933-3413 from Monday-Friday, 8 a.m. to 8 p.m. Eastern Standard Time.

This reference document should be kept readily available in the office of all health care providers that serve women, adolescents, and children. The summarized recommendations are provided for quick reference; however, the full version of this document is written in a manner that supports a comprehensive approach to caring for HIV positive pregnant women and perinatally HIV exposed children.

For a copy of this document visit the Michigan Department of Community Health website at: www.michigan.gov/mdch.

INTRODUCTION

LESSONS LEARNED

Since the release of the first edition of Improving the Odds, many lessons have been learned both locally and nationally. National data has shown many women, especially those who used illicit drugs, were not tested for HIV during pregnancy due to lack of prenatal care (PNC). In addition, many women refused testing because their health care providers did not strongly recommend it. Some women declined testing because of perceived low risk. Some providers did not offer testing because of perceived low risk, perceived difficulties and complexity of required counseling, and misunderstanding of counseling requirements.⁽¹⁾

Continued efforts are needed to assist pregnant women to obtain prenatal care and to provide them with HIV counseling and testing. In Michigan, 10% of HIV-infected pregnant women received no PNC, compared with 1% in the general population. The high prevalence of sexually transmitted diseases, illegal drug, and alcohol use among HIV positive women giving birth in Michigan, suggests that medical practitioners need to provide treatment or appropriate care referrals for HIV positive women to manage their HIV infection, substance abuse, and other co-morbid conditions and to prevent perinatal HIV transmission.⁽²⁾ In Michigan, perinatally HIV exposed infants have become infected with HIV due to the mother's unidentified HIV status during prenatal care or at the time of labor and delivery.

NATIONAL TRENDS

Of the estimated 886,575 Americans that have been diagnosed with HIV/AIDS from the beginning of the epidemic through 2002, 159,271 of those have occurred in adolescent (> 13 years) and adult females. Women account for one of the most rapid increases in cases of HIV/AIDS reported to the CDC. The CDC reports that in 1990 women and adolescent girls accounted for 11% of total AIDS cases. By 2002, this group accounted for 26% of all AIDS cases diagnosed in the United States. From 1998 through 2002 the number of AIDS cases diagnosed increased 7% among women. According to the CDC women across all racial and ethnic groups most commonly report heterosexual contact or injection drug use as their primary modes of HIV exposure. As of 2002, of the 82,764 adolescent and adult female AIDS cases, 61% or 50,174 were attributed to heterosexual contact and 36% or 30,158 were attributed in injection drug use. Furthermore, HIV/AIDS was the third leading cause of death for women ages 35-44 in 2001 and the leading cause of death among African American women ages 25-34.^(3, 4)

As the incidence of HIV/AIDS increases among women of child bearing age, increasing number of children are exposed and possible infected through perinatal i.e., mother to child transmission (MTCT). The CDC estimates there are between 280-370 perinatal HIV transmissions that occur each year in the United States. As of 2002, of the 3,893 children less than age thirteen living with AIDS, 96% or 3,748 were infected via MTCT.^(3,5)

In the absence of medical intervention, the risk of MTCT is 15 to 30%, with estimates ranging from 13-45%. Infection is acquired in utero 20-30% of the time, and 70-80% of transmission occurs in the peripartum period. Since the advent of ZDV chemoprophylaxis and other measures, transmission risks have been reduced to 2-3% and there is increasing evidence that optimized antiretroviral therapy can achieve a transmission risk of 0%. Breast-feeding also contributes to an increased risk of transmission.

MICHIGAN TRENDS

Women Living with HIV/AIDS

As of January 1, 2004, the Michigan Department of Community Health HIV, STD and Bloodborne Infections Surveillance Section estimates that there are 16,200 people living with HIV or AIDS in the State of Michigan. Michigan ranked 17th nationally in the total number of AIDS cases reported (12,645) and ranked 30th by annual rate per 100,000 population (127.2). Each county in Michigan has persons living with HIV or AIDS, with the greatest number of people living with HIV or AIDS residing in Wayne County, including the City of Detroit, Oakland, Kent, Genesee, Macomb, Kalamazoo, Ingham, and Washtenaw counties.

Data from the MDCH HIV, STD and Bloodborne Infections Surveillance Section show there are 2,532 (23%) women living with HIV or AIDS in Michigan. There are 1,571 women ages 30 and older living with HIV or AIDS. Between the ages of 20-29 years, 767 women are living with HIV or AIDS. There are 121 women aged 13-19 living with HIV or AIDS. For females younger than twelve years of age, there are 71 living with HIV or AIDS. (Ages for two women were not available and therefore the total for the age breakdown equals 2,530.)

In Michigan, HIV/AIDS disproportionately affects African-American women. African-American women account for 73% of the cases among women living with HIV or AIDS. This compares to 22% for White women, 4% Hispanic women, and 2% for women of other or unknown races. Of the 1,837 African American women living with HIV/AIDS in Michigan, 747 (41%) became infected through heterosexual sex. (The definition of a high-risk heterosexual partner includes: an injecting drug user, bisexual male, known HIV positive partner, or a partner who had a blood exposure.) The other main risk behaviors for African American women include: injecting drug use (529/29%) and presumed heterosexual sex (418/23%). Of the 547 White women living with HIV/AIDS in Michigan, 283 (53%) became infected through heterosexual sex. The other main risk behaviors for White women include: injecting drug use (129/24%) and presumed heterosexual sex (97/18%). Of the 92 Hispanic women living with HIV/AIDS in Michigan, 55 (60%) became infected through heterosexual sex. The other main risk behaviors for Hispanic women include: injecting drug use (15/16%) and presumed heterosexual sex (15/16%).⁽⁶⁾

Perinatally HIV Exposed and HIV Positive Infants

The number of perinatally HIV exposed children that have become HIV infected in Michigan has fluctuated since 1994 when the results of the AIDS Clinical Trials Group (ACTG) documented that ZDV chemoprophylaxis could reduce perinatal HIV-1 transmission by nearly 70%. Data in the Mortality and Morbidity Weekly Report, "Progress Toward Elimination of Perinatal HIV Infection—Michigan, 1993-2000", indicated a high proportion of health care providers are following the Public Health Service Guidelines for maternal and neonatal ZDV use to reduce perinatal HIV transmission. Michigan health care providers are also using highly active antiretroviral therapy

(HAART), which lowers maternal viral load and contributes to a decreasing transmission rate. However, continued efforts are needed to assist pregnant women to obtain prenatal care and to provide them with HIV counseling and testing.⁽⁷⁾

The failure of health care providers to offer pregnant women HIV counseling and testing and therefore the failure to identify the woman as being HIV positive during pregnancy is the main reason perinatally HIV exposed children in Michigan have become infected with HIV. The opportunity to prevent MTCT through the administration of maternal ZDV during pregnancy and/or at labor and delivery and to the neonate is lost without the identification of the mother being HIV positive. Epidemiological data from the MDCH HIV, STD and Blood borne Infections Surveillance Section has confirmed 599 perinatally HIV exposed children born from 1994-2003. Of the 599 perinatally HIV exposed children, 58 (10%) were infected via MTCT. Of the 58 HIV positive children, data was available on 55 of the mothers. Of the 55 mothers, only 20 (36%) had their HIV status confirmed prior to delivery. Another 3 (5%) women were identified as HIV positive in labor and delivery. The remainder of the women were not identified as being HIV positive in a timely manner to initiate HAART for her own health and for the reduction of MTCT. Furthermore, of the 55 women, only 8 (7%) received ZDV during pregnancy and/or at labor and delivery.⁽⁸⁾ Regarding neonatal ZDV only 14 (25%) of the HIV perinatally exposed children (with an identified mother) received neonatal ZDV.

MATERNAL HIV COUNSELING AND TESTING

MICHIGAN PUBLIC HEALTH CODE 333.5123-PRENATAL HIV COUNSELING AND TESTING

Since 1989, Michigan law has required testing of pregnant women for HIV, hepatitis B, and other sexually transmitted diseases at the time of initial examination, unless the woman does not consent or if the tests are medically contraindicated. Section 333.5123 of Michigan's Public Health Code declares: "A physician or an individual otherwise authorized by law to provide medical treatment to a pregnant woman shall take or cause to be taken, at the time of the woman's initial examination, test specimens of the woman and shall submit the specimens to a clinical laboratory approved by the department for the purpose of performing tests approved by the department for venereal disease (syphilis), HIV or an antibody to HIV, and for hepatitis B. If, when a woman presents at a health care facility to deliver an infant or for care in the immediate postpartum period having recently delivered an infant outside a health care facility, no record of results from the tests required by this subsection is readily available to the physician or individual otherwise authorized to provide care in such a setting, then the physician or individual otherwise authorized to provide care shall take or cause to be taken specimens of the woman and shall submit the specimens to a clinical laboratory approved by the department for the purpose of performing department approved tests for venereal disease (syphilis), for HIV or an antibody to HIV, and for hepatitis B. This subsection does not apply if, in the professional opinion of the physician or other person, the tests are medically inadvisable or the woman does not consent to be tested."⁽⁹⁾

In 1994, the law was expanded to include voluntary testing at the time of delivery or immediate postpartum if no previous testing is documented in the medical records. To comply with Michigan law, health care providers must offer all pregnant women HIV counseling and testing regardless of a woman's age, marital status, parity, race, or socioeconomic status.

In April 2003 the CDC issued a "Dear Colleague" letter promoting an "opt-out" approach to maternal HIV testing, in which pregnant women are notified that an HIV test will be routinely included in the standard battery of tests for all pregnant women, unless they decline testing.⁽¹⁰⁾ MDCH recommends that clinicians comply with the Michigan Public Health Code 333.5123-Prenatal HIV Counseling and Testing, and routinely include HIV testing in the standard battery of tests for all pregnant women, with written informed consent, unless the woman refuses or the test is medically inadvisable. MDCH recognizes that pre and post test counseling may act as a barrier to routinized HIV testing for pregnant women and therefore recommends the minimal amount of information be given to the woman as outlined by the CDC, which can be found on page 10 of this document.

MICHIGAN DEPARTMENT OF COMMUNITY HEALTH RECOMMENDATIONS

The Michigan Department of Community Health recommends that maternal HIV information based counseling and testing should be a routine part of a woman's prenatal care unless the woman refuses or the test is deemed medically inadvisable. Under this opt-out approach pregnant women are notified that a HIV test will be included in the standard battery of tests for all pregnant women. Women must sign consent for testing which should be documented in her medical record. If a woman refuses testing, it must be documented in medical record. MDCH also makes the following recommendations to ensure HIV information based counseling and testing is offered to all pregnant women.⁽¹¹⁾

CLINICAL PATHWAYS

1. HIV testing and information based counseling should be components of a health care facility's clinical pathways. Attending and resident physicians, nurses, nurse practitioners, physician assistants, and any other health care worker providing services to pregnant women need to be trained on providing HIV information based counseling and testing, hepatitis B testing and syphilis testing, as Michigan's Public Health Code requires.
2. Health care facilities should have policies and procedures in place to ensure that the clinical pathways are being followed.

PRENATAL TESTING

1. Physicians providing medical treatment to pregnant women are required, at the time of initial examination to offer testing for HIV. Information based counseling should be provided at that time. Documentation of consent to test or refusal to test in the woman's medical chart is required in accordance with Michigan's Public Health Code.
2. Exemptions for HIV testing include:
 - a. The woman does not consent to the testing.
 - b. The physician deems the test(s) medically inadvisable.
3. Women who test positive for HIV or who refuse testing should:
 - a. not be denied prenatal or other health care service,
 - b. receive assurance that they will not be reported to child protective service agencies, nor lose custody of their children, because of refusal to be tested or because of their HIV status,
 - c. not be discriminated against in any other way.
4. If a woman tests negative for HIV at the time of her initial examination, but continues to engage in behaviors that place her at risk for contracting HIV, she should be offered HIV counseling and testing in the third trimester, preferably before 36 weeks of gestation. HIV testing should also be offered at the time of delivery if there is not the opportunity to test the woman in the third trimester of pregnancy or if her HIV status is unknown to the labor and delivery provider.
5. If the patient has not received prenatal care or her test results are not available prior to admission for labor and delivery, then HIV testing must be performed at delivery, keeping in mind the previously noted exemptions. For women who are first identified as being HIV infected during labor and delivery, health care providers should offer intrapartum and neonatal ZDV according to published recommendations.
6. If a woman presents in the immediate postpartum period and there are no records of her test results available, then tests for HIV must be performed, keeping in mind the previously noted exemptions.
7. Documentation of testing, and/or refusal to test, must be made in the woman's medical record.
8. If the tests are not performed, the physician is required by law to document the reason(s) for not testing.
9. Health care providers must routinely offer HIV testing counseling to all pregnant women. They should not deny the woman the opportunity for HIV testing based on their beliefs or what they may perceive as the patient's risk factors for HIV infection.
10. In order that HIV counseling and testing be readily available to all women, specific strategies and resources will be needed to communicate with women who may not obtain or adhere to prenatal care because of homelessness, incarceration, undocumented citizenship status, drug or alcohol abuse, or other reasons. Health care providers should be aware of the complex issues that HIV infected women must consider about their reproductive options, and reproductive counseling should be non-directive.
11. Pregnant women, regardless of their infection status, should be provided access to other HIV prevention and treatment services (e.g., substance abuse treatment, partner counseling and referral services, case management, mental health services, etc.) as needed. For a comprehensive list of services, see the referral section on page 46 or contact AIDS Partnership Michigan at 1-800-872-2437 for the HIV/AIDS and Hepatitis C Resource Guide, or Friends Alliance at 1-800-350-7927 for copies of the PWH/A Pocket Reference Guide, or visit their website at: <http://www.friendsalliance.org>.

12. Referrals should be made at the time the woman receives counseling. Health care providers should ensure that appointments are made. Health care providers should make the follow-through process as easy as possible for women by providing clear instructions on where they are to go and make appointments to facilities that are accessible to the client. Efforts should be made to make counseling and testing easily available, including use of mobile units, the use of community-based organizations and other appropriate agencies.

HIV TESTING OTHER CHILDREN

HIV testing should be considered for babies and older children of women who are HIV positive or whose HIV status is unknown and who have engaged in risk behaviors. Testing should be done in accordance with prevailing legal requirements and with the consent of the legal guardian. Foster care does not change guardianship. The guardian must consent. Counseling should include the risks for HIV, the benefits to knowing a child's infection status, the need for follow-up and early medical intervention in the event the child tests positive, and the understanding that a positive HIV test in a baby is indicative of infection in the mother. Foster care agencies must assure referral for early medical intervention and monitoring when indicated for HIV-positive children in their care.

CDC REVISED GUIDELINES FOR HIV COUNSELING, TESTING, AND REFERRAL AND REVISED RECOMMENDATIONS FOR HIV SCREENING OF PREGNANT WOMEN MMWR 2001;50 (NO. RR 19): 1-58⁽¹²⁾

(Adopted from the CDC. Revised Guidelines for HIV Counseling, Testing, and Referral and Revised Recommendations for HIV Screening of Pregnant Women. MMWR 2001;50 (No. RR 19): 1-58)

1. The Public Health Service recommends that all pregnant women in the United States be tested for HIV infection. All health-care providers should recommend HIV testing to all of their pregnant patients, pointing out the substantial benefit of knowledge of HIV status for the health of women and their infants. HIV screening should be a routine part of prenatal care for all women.
2. HIV testing should be voluntary and free of coercion. Informed consent before HIV testing is essential. Information regarding consent can be presented orally or in writing and should use language the client understands. Accepting or refusing testing must not have detrimental consequences to the quality of prenatal care offered. Documentation of informed consent should be in writing, preferably with the client's signature. State or local laws and regulations governing HIV testing should be followed. HIV testing should be presented universally as part of routine services to pregnant women, and confidential informed consent should be maintained (see www.cdc.gov/mmwr/preview/mmwrhtml/rr5019a1.htm for the *Revised Guidelines for HIV Counseling, Testing, and Referral*).
3. Although HIV testing is recommended, women should be allowed to refuse testing. Women should not be tested without their knowledge. Women who refuse testing should not be coerced into testing, denied care for themselves or their infants, or threatened with loss of custody of their infants or other negative consequences. Discussing and addressing reasons for refusal (e.g., lack of awareness of risk or fear of the disease, partner violence, potential stigma, or discrimination) could promote health education and trust building and allow some women to accept testing at a later date. Women who refuse testing because of a previous history of a negative HIV test should be informed of the importance of retesting during pregnancy. All logistical reasons for not testing (e.g., scheduling) should be addressed as well. Health-care providers should remember that some women who initially refuse testing might accept at a later date, particularly if their concerns are discussed. Some women who refuse confidential testing might be willing to obtain anonymous testing. However, they should be informed that if they choose anonymous testing, no documentation of the results will be recorded in the medical chart, and their providers might have to retest them, potentially delaying provision of antiretroviral drugs for therapy or perinatal prophylaxis. Some women will continue to refuse testing, and their decisions should be respected.
4. **Before HIV testing, health-care providers should provide the following minimum information.** Although a face-to-face counseling session is ideal, other methods can be used (e.g., brochure, pamphlet, or video) if they are culturally and linguistically appropriate.

- a. HIV is the virus that causes AIDS. HIV is spread through unprotected sexual contact, injection-drug use, MTCT, and breast feeding. Approximately 25% of HIV-infected pregnant women who are not treated during pregnancy can transmit HIV to their infants during pregnancy, during labor and delivery, or through breast-feeding.
 - b. A woman might be at risk for HIV infection and not know it, even if she has had only one sex partner.
 - c. Effective interventions (e.g., highly active combination antiretrovirals) for HIV-infected pregnant women can protect their infants from acquiring HIV and can prolong the survival and improve the health of these mothers and their children.
 - 1. For these reasons, HIV testing is recommended for all pregnant women.
 - 2. Services are available to help women reduce their risk for HIV and to provide medical care and other assistance to those who are infected.
 - 3. Women who decline testing will not be denied care for themselves or their infants.
5. Health-care providers should perform HIV testing in consenting women as early as possible during pregnancy to promote informed and timely therapeutic decisions. Retesting in the third trimester, preferably before 36 weeks of gestation, is recommended for women known to be at high risk for acquiring HIV (e.g., those who have a history of sexually transmitted diseases [STDs], who exchange sex for money or drugs, who have multiple sex partners during pregnancy, who use illicit drugs, who have sex partner[s] known to be HIV-positive or at high risk, and who have signs and symptoms of seroconversion). Routine universal retesting in the third trimester may be considered in health-care facilities with high HIV seroprevalence among women of childbearing age. Retesting for syphilis during the third trimester and again at delivery is also recommended for pregnant women at high risk (see www.cdc.gov/mmwr/preview/mmwrhtml/00050909.htm for the 1998 Guidelines for Treatment of Sexually Transmitted Diseases). Some states mandate syphilis screening at delivery for all pregnant women.
 6. Women admitted for labor and delivery with unknown or undocumented HIV status should be assessed promptly for HIV infection to allow for timely prophylactic treatment. Expedited testing by either rapid return of results from standard testing or use of rapid testing (with confirmation by a second licensed test when available) is recommended for these women. The goal is to identify HIV-infected women or their infants as soon as possible because the efficacy of prophylactic therapy is greatest if given during or as soon after exposure as possible (i.e., within 12 hours of birth). Informed consent is essential for women tested prenatally, and women in labor with unknown status should be allowed to refuse testing without undue consequences. After delivery, standard confirmatory testing should be done for women with positive rapid test results.
 7. Some women may not: a) receive testing during labor and delivery, b) choose to be tested for HIV, or c) retain custody of their infants. If the mother has not been tested for HIV, she should be informed that knowing her infant's infection status has benefits for the infant's health and that HIV testing is recommended for her infant. Providers should ensure that the mother understands that a positive HIV antibody test for her infant indicates infection in herself. For infants whose HIV infection status is unknown and who are in foster care, the person legally authorized to provide consent should be informed that HIV testing is recommended for infants whose biological mothers have not been tested. Testing should be performed in accordance with the policies of the organization legally responsible for the child and with prevailing legal requirements for HIV testing of children.
 8. Regulations, laws, and policies regarding HIV screening of pregnant women and infants are not standardized throughout all states and U.S. territories. Health-care providers should be familiar with and adhere to state/local laws, regulations, and policies concerning HIV screening of pregnant women and infants.

BENEFITS OF UNIVERSAL COUNSELING AND VOLUNTARY TESTING OF PREGNANT WOMEN

HIV PREVENTION AND TREATMENT OPPORTUNITIES FOR WOMEN AND INFANTS

1. HIV counseling and testing for women of childbearing age offer important prevention opportunities for both uninfected and infected women and their infants. Such counseling is intended to:

- a. Assist women in assessing their current or future risk for HIV infection;
 - b. Initiate or reinforce HIV risk reduction behavior; and
 - c. Allow for referral to other HIV prevention services (e.g., treatment for substance abuse and sexually transmitted diseases) when appropriate.
2. For HIV positive women, knowledge of their HIV infection status provides opportunities to:
- a. Obtain treatment for themselves and diagnosis and treatment for their infants;
 - b. Make informed reproductive decisions;
 - c. Use methods to reduce the risk for perinatal transmission;
 - d. Receive information to prevent HIV transmission to others; and
 - e. Obtain referral for psychological and social services, as needed.
3. Interventions designed to reduce morbidity in HIV positive persons require that HIV be diagnosed so treatment can be initiated in a timely manner.
4. Providing HIV counseling and testing services in gynecologic, prenatal and other obstetric settings presents an opportunity for early diagnosis of HIV, since many women only access the health care system for obstetric or gynecologic-related care.

HIV REPORTING

Section 333.5111 of Michigan's Public Health Code (Act No. 368 of the Public Acts of 1978, as amended) requires physicians and other health care professionals to report HIV, AIDS, hepatitis B and syphilis.⁽¹³⁾ All reporting forms are available from the local health department and/or the Michigan Department of Community Health.

1. Individuals who test positive for HIV infection (repeatedly reactive ELISA and Western blot confirmed) must be promptly reported to local health authorities on the CDC's Pediatric (for persons <13 years of age at time of diagnosis) or "Adult HIV/AIDS Confidential Case Report" form - 50.42A (adult cases) or 50.42B (pediatric cases). Adult patients can be reported anonymously. (This applies to adult HIV reporting in the outpatient setting only except for purposes of PCRS - see section on PCRS below.) According to Michigan's Public Health Code the report of HIV infection does not need to include the name, address, and phone number of the test subject if:
 - a. The patient undergoes the test in a physician's private office or the office of a physician employed by or under contract with a HMO; and
 - b. The patient requests that this information not be included in the report. If making the report anonymously, the top section should be left blank.
2. All children perinatally exposed to HIV and children that test positive for HIV must be reported by name to the local health authorities on CDC's "Pediatric HIV/AIDS Confidential Case Report" Form (50.42B)

PARTNER COUNSELING AND REFERRAL SERVICES (PCRS)

MCL 335.5131 of the Michigan Public Health Code (Public Act 488 of 1988 as amended by Act 96 of 1992) places an affirmative duty upon physicians and local health officers to notify known sexual or needle sharing partners of HIV infected patients about their potential exposure to HIV. However, physicians and local health officers may discharge this duty to Partner Counseling and Referral Services at the local health department.

Persons making the notification to the contact may not disclose the identity of the patient to the contact unless the HIV infected individual has provided written consent for this disclosure, and if the release of the patient's name is reasonably necessary to prevent a foreseeable risk of HIV transmission.

INTERPRETATION OF HIV TEST RESULTS

1. HIV antibody testing should be performed according to current recommendations, which includes the use of an enzyme immunoassay (EIA) to test for antibody to HIV and confirmatory testing with an additional, more specific assay (i.e., Western blot or immunofluorescence assay [IFA]). All assays should be performed and conducted according to manufacturers' instructions and applicable state and federal laboratory guidelines.
2. HIV infection (as indicated by the presence of antibody to HIV) is defined as a repeatedly reactive EIA and a positive confirmatory supplemental test, such as a Western Blot or a positive PCR. Women with persistent indeterminate test results should be referred for further definitive antigen based testing (i.e. PCR). Pregnant women who have repeatedly reactive EIA and indeterminate supplemental tests should be retested immediately for HIV antibody to distinguish between recent seroconversion and a negative test result. Women with a positive test should always be retested to confirm their positive status. Uncertainties regarding HIV infection status should be resolved before final decisions are made concerning pregnancy termination, ZDV therapy, or other interventions.
3. Women who have negative EIAs and those who have repeatedly reactive EIAs, but negative confirmatory tests, should be considered uninfected.
4. Pregnant women with negative tests should receive a full explanation of what a negative test means and include that explanation in the context of the client's risk.
5. For women who did not receive prenatal care or were not offered HIV counseling and testing and their HIV status is not known at the time of labor and delivery, a rapid 20-minute screening tests for HIV antibody may be performed either in a clinical laboratory or at the bedside (using the CLIA-exempted OraQuick test on capillary or venous blood or oral mucosa). A positive HIV screening must be followed by standard screening and confirmatory tests over the next 48 hours. A single positive screening test will accurately predict HIV infection in populations of moderate or high prevalence; however, there is a risk of false-positive results in populations of low HIV prevalence. Institutions providing obstetrical deliveries should make an informed decision, based on local epidemiology, as to the potential benefit of implementing rapid screening during labor for women without HIV test results.

RECOMMENDATIONS FOR HIV POSITIVE PREGNANT WOMEN

1. HIV positive pregnant women should receive counseling and testing as recommended in the 2004 CDC Revised Recommendations For HIV Screening of Pregnant Women. Post test HIV counseling should include an explanation of the clinical implications of a positive HIV antibody test result and the need for, benefit of, and means to access HIV related medical and other early intervention services. Such counseling should also include a discussion of the interaction between pregnancy and HIV infection, the risk for perinatal HIV transmission and ways to reduce this risk, the prognosis for infants who become infected, and available existing support services and reasonable linkages with those services.
2. HIV infected pregnant women should be evaluated according to published recommendations to assess their need for antiretroviral therapy, antimicrobial prophylaxis, and treatment of other conditions. Although medical management of HIV infection is essentially the same for pregnant and non-pregnant women, recommendations for treating a patient who has tuberculosis have been modified for pregnant women because of potential teratogenic effects of specific medications (e.g., streptomycin and pyrazinamide). HIV infected pregnant women should be evaluated to determine their need for psychological and social services, and referrals made as appropriate. All providers including managed care providers should ensure that support services are available to women.
3. HIV infected pregnant women should have access to the same combination antiretroviral treatment, based on their immunologic and virologic status, as non-pregnant HIV positive women. Special issues to consider in the use of antiretroviral therapy during pregnancy are potential toxicities to the fetus, especially during the first trimester; known safety considerations regarding use of specific agents during pregnancy; and changes in pharmacokinetics during pregnancy. These issues are discussed in greater detail in Section Two. Consultation with an expert in the use of these medications during pregnancy is strongly recommended.
4. HIV infected pregnant women should be provided information concerning interventions to reduce perinatal transmission, including ZDV as part of their combination antiretroviral therapy, and elective Cesarean section. This information should

address the potential benefit, as well as, known and unknown short term and long term risks of these interventions to the woman and her child.

5. HIV positive pregnant women should be encouraged, but not coerced, into using these interventions as applicable. Decisions should be made after consideration of both the benefits and potential risks of the regimen to the woman and her child. Therapy should be offered according to the appropriate regimen in published recommendations. A woman's decision not to accept treatment should not result in punitive action or denial of care.
6. HIV positive pregnant women should receive information about all reproductive options. Health care providers should be aware of the complex issues that HIV infected women must consider when making decisions about their reproductive options, and reproductive counseling should be non-directive.
7. To reduce the risk for HIV transmission to their infants, HIV positive women should be advised against breast-feeding. Support services should be provided when necessary for use of appropriate breast milk substitutes. This includes available supplemental food programs, such as Women Infants and Children (WIC). To contact the nearest WIC agency, call 1-800-26-BIRTH or e-mail WIC at: MichiganWIC@michigan.gov.
8. Confidential HIV related information should be disclosed or shared only in accordance with Michigan law. To optimize medical management and comply with current law, counseling and testing acceptance or refusal should be documented. Positive or negative HIV test results should be available to a woman's health care provider and included on both her and her infant's confidential medical records. Providers should obtain from the mother a written release of information, specific for HIV-related information, which includes to whom, for what purposes, and for how long information will be released. After consulting with the mother, maternal health care providers should notify the pediatric care providers of the impending birth of an HIV exposed child, any anticipated complications, and whether ZDV should be administered after birth. If HIV is first diagnosed in the child, the child's health care providers should discuss the implication of the child's diagnosis and assist the mother in obtaining HIV counseling and testing and health care for herself.
9. Counseling for HIV infected pregnant women should include an assessment of the potential for negative effects resulting from HIV infection (e.g., discrimination, domestic violence, and psychological difficulties). For women who anticipate or experience such effects, counseling also should include:
 - a) information on how to minimize these potential consequences,
 - b) assistance in identifying supportive persons within their own social network; and
 - c) referral to appropriate psychological, social, and legal services.
10. HIV infected women should be encouraged to allow HIV testing of any of their children born after they became infected or after 1977 if they do not know when they became infected. Women should be informed that the lack of signs and symptoms suggestive of HIV infection in older children does not necessarily indicate a lack of HIV infection; some perinatally infected children can remain asymptomatic for many years.

RECOMMENDATIONS FOR FOLLOW-UP OF POSITIVE WOMEN AND PERINATALLY EXPOSED INFANTS

1. Following pregnancy, HIV positive women should be followed by a health care professional skilled in providing HIV medical care to HIV positive women. Ongoing HIV related medical care should include: immunological and virologic monitoring, antiretroviral therapy, prophylaxis for and treatment of opportunistic infections and other HIV related conditions, and screening for hepatitis B and C. HIV positive women should also receive gynecologic care, including regular Pap smears, reproductive counseling, information on how to prevent sexual transmission of HIV and other STDs and treatment of gynecologic conditions according to published recommendations.
2. HIV positive women who are using illicit drugs or are alcohol dependent should be assessed for substance abuse treatment readiness and referred appropriately.
3. HIV positive women (or the guardians of their children) should be informed of the importance of follow-up for their children. These children should receive follow-up care to continue prophylaxis with antiretrovirals, such as ZDV for the first six weeks

of life, in accordance with the perinatal intervention agreed upon by the mother. In addition, follow-up is necessary to ascertain the child's HIV status, to initiate prophylactic therapy to prevent PCP or other opportunistic infections if indicated, to determine the need for antiretroviral and other prophylactic therapy and to initiate regular pediatric care. HIV positive children and other children living in households with HIV positive persons should be vaccinated according to published Recommendations of the Advisory Committee on Immunization Practices (ACIP). <http://www.cdc.gov/nip/acip>.

4. Permanency planning should be considered for every parent and or caregiver of an HIV exposed or HIV positive child. Permanency planning can be discussed with a case manager and/or social worker.
5. For children in foster care that have never been tested and their mother has tested HIV positive since their birth and/or they have a HIV exposed and/or infected sibling, the child in foster care needs to be tested for HIV. Under the MCL 333.5131 Confidentiality of HIV/AIDS Information, disclose of a foster child's serostatus is allowed if the foster parent is the legal guardian. Only the Family Independence Agency, the State Department of Community Health, the Probate Court, or a child placement agency can make such a disclosure to the foster parents.⁽¹⁴⁾

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CLINICAL GUIDELINES TO REDUCE PERINATAL HIV TRANSMISSION

INTRODUCTION

Among the most dramatic successes in HIV prevention is the ability, since 1994, to drastically reduce mother to child transmission. In the early 1990's approximately 7,000 HIV infected women gave birth annually in the United States. Given an average transmission rate of about 25%, between 1,000 and 2,000 HIV infants were born each year. Currently, the CDC estimates that 280-370 infants are born with HIV infection each year in the United States.

In 1994, the results of the landmark study, AIDS Clinical Trial Group (ACTG) Study 076, were published in the *New England Journal of Medicine*. A course of oral Zidovudine (ZDV or Retrovir) taken by the mother during the second and third trimesters, along with intravenous ZDV given as a constant infusion during labor and delivery, and followed by 6 weeks of oral antiretroviral treatment to the newborn, reduced the transmission rate from 25% in the control mother-infant pairs to 7.6% in the antiretroviral recipients. All children received artificial feeding, and thus were not exposed to HIV via maternal milk. There was negligible short-term toxicity, with modest and transient anemia occurring in the ZDV treated infants. Implementation of this protocol rapidly became the standard of care in developed nations. HIV testing during pregnancy was strongly promoted so that HIV positive women could be diagnosed and avail themselves of this powerful prophylactic regimen.

Since 1994, combination antiretroviral therapy including potent drugs from the protease-inhibitor and non-nucleoside reverse transcriptase inhibitor class reduced mortality from HIV/AIDS in developed nations almost 80%. Potent combination antiretroviral therapy, reducing plasma HIV RNA levels to less than 1000 copies/mL, combined with intrapartum and postpartum ZDV (per the ACTG 076 regimen) has reduced perinatal transmission to between zero and 2% in several studies. In addition, observational studies and a randomized controlled trial demonstrated that elective Caesarian section, performed before the onset of labor or rupture of membranes, reduced perinatal transmission in women receiving less intensive antiretroviral therapy between 50 and 75%.

Now there are four powerful interventions to reduce HIV transmission from mother to child: the three-phase ZDV regimen; potent combination antiretroviral therapy; scheduled Caesarean section; and artificial infant feeding. In addition, short-course intervention with antiretroviral therapies have demonstrated effectiveness in studies in developing countries. Several of these short-course regimens

provide options to intervene successfully with women in labor and their newborns, if the mothers have not used antiretroviral therapy during their pregnancy. These guidelines describe interventions in greater detail, to equip the obstetric, pediatric and primary care providers of Michigan with the tools to bring perinatal transmission near zero.

The Michigan Department of Community Health would like to thank: Dr. Jonathan Cohn, Associate Professor of Medicine, Wayne State University School of Medicine, Department of Medicine, Division of Infectious Diseases, Dr. Theodore Jones, Associate Professor of OB/GYN, Associate Chair for Education, Director OB/GYN Residency Program Wayne State University School of Medicine, Department of Obstetrics and Gynecology, Division of Maternal/Fetal Medicine; and Dr. Ellen Moore Associate Professor of Pediatrics Wayne State University, Chief of the Division, and Allergy, Immunology, and Rheumatology, Children's Hospital of Michigan for their clinical expertise in revising the clinical guideline section of Improving the Odds.

PRECONCEPTUAL COUNSELING AND CARE FOR HIV-1 INFECTED WOMEN

(Adopted from the Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States MMWR 1998/47(RR-2); 1-30.)

The American College of Obstetrics and Gynecology advocates extending all women of childbearing age the opportunity to receive preconception counseling as a component of routine primary medical care. Preconception care can identify risk factors for adverse maternal or fetal outcomes, provide education and counseling targeted to the woman's needs, and treat or stabilize medical conditions before conception to optimize maternal and fetal outcomes.

For HIV positive women, preconception care must also focus on maternal infection status, viral load, immune status, and the therapeutic regimen. Education regarding perinatal transmission risk and prevention strategies, expectations for the child's future, and effective contraception should also be discussed. The following components of preconception counseling are recommended for HIV positive women:

1. Selection of effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy.
2. Education and counseling regarding perinatal transmission risks, strategies to reduce those risks and potential effects of HIV, or treatment on the pregnancy and outcomes.
3. Initiation or modification of antiretroviral therapy:
 - Avoid agents with potential reproductive toxicity for the developing fetus (e.g. efavirenz, hydroxyurea)
 - Choose agents effective in reducing the risk of perinatal HIV-1 transmission
 - Attain a stable, maximally suppressed maternal viral load
 - Evaluate and control for therapy associated with side effects, which may adversely impact the maternal-fetal health outcomes (hyperglycemia, anemia, hepatic toxicity)
4. Evaluation and appropriate prophylaxis for opportunistic infections and administration of medical immunizations (influenza, pneumococcal, or hepatitis B vaccines) as indicated.
5. Optimization of maternal nutritional status.
6. Institution of the standard measures for preconception evaluation and management (e.g. assessment of reproductive and family genetic history, screening for infectious diseases/sexually transmitted diseases, and initiation of folic acid supplementation).
7. Screening for maternal psychological and substance abuse disorders.
8. Plan for perinatal consultation as indicated.

HIV positive women of childbearing age receive their primary health care in a variety of clinical settings, such as family planning, family medicine, internal medicine, and obstetrics/gynecology practices. It is imperative that primary health care providers consider the principals of preconception counseling as an integral component of their comprehensive primary health care for improving maternal/child health outcomes.

IDENTIFICATION OF PREGNANT WOMEN WITH HIV INFECTION AND DOCUMENTATION OF MATERNAL HIV ANTIBODY STATUS

At least one third of the perinatal transmissions in recent years occurred in infants born to women unaware of their HIV infection. Many of these women do not consider themselves to be at risk, as they are often monogamous and without high-risk behavior except for unprotected intercourse with their partner. Although a sensitive topic, the ability to insure monogamy in a relationship cannot be guaranteed. In addition, a health care provider may not consider these women to be at risk and may not thoroughly discuss risks of sexual transmission. Aiming at zero perinatal transmission requires that every pregnant woman be offered HIV testing as part of routine prenatal care.

Other women, who many clinicians would recognize as being at risk for HIV, may be reluctant to participate in prenatal care. They include women injecting drugs, women engaging in commercial sex, or women with partners who themselves have high-risk behaviors. Clinical sites that serve women with these behaviors have a special challenge to win the trust and participation of their patients in aiming at zero perinatal transmission.

All obstetricians, midwives, family practitioners, and other prenatal care providers should counsel every pregnant woman about the benefits of knowing her HIV status. She can then make an informed decision about being tested. All health care providers for women should routinely offer and recommend HIV antibody testing for all pregnant women and all women considering pregnancy. Testing should be performed as early as possible during pregnancy. Pregnant women with on-going high risk behavior during pregnancy should be offered re-testing in the third trimester if negative on initial screening.

Current federal and state policy and law are shaped largely in response to the seminal results of the ACTG 076. During admission for labor and delivery, routine history taking should include determination of HIV serostatus. Their assessment for HIV infection should elicit information regarding prior HIV testing, test results, and risk history. The Prenatal Care Requirement of the Michigan Law (Act 491 of 1988, as amended by Act 200 of 1994-Section 5123) requires that:

Pregnant women be offered counseling and be tested for HIV, hepatitis B, and venereal disease (syphilis) at the time of the woman's first prenatal visit unless the tests are medically inadvisable, or the woman refuses consent to be tested. If the woman has not been previously tested, and she presents at a health care facility for delivery, or for care in the immediate postpartum period following delivery outside of a health care facility, and her results are unknown or unavailable the law also states that the women should be tested unless medically inadvisable, or if she refuses consent.

(For the complete language of 333.5123, refer to Section 1, Maternal HIV Counseling and Testing, page 5.)

If the institution where the pregnant woman delivers cannot document HIV serostatus, it is necessary for the women to receive HIV counseling and be offered testing as soon as the mother's medical condition permits. This is especially important in women who have received no prenatal care, since the prevalence of HIV infection may be higher in these women. For those women who are known to be HIV infected, a history of prenatal antiretroviral use should also be obtained in order to facilitate intrapartum treatment. In situations where medical documentation of maternal infection is not available and the woman states that she is HIV infected, therapy may be offered and initiated while awaiting serological confirmation.

Rapid 20-minute screening tests for HIV antibody may be performed either in a clinical laboratory or at the bedside (using the CLIA-exempted OraQuick test on capillary or venous blood or oral mucosa). A positive HIV screening must be followed by standard screening and confirmatory tests over the next several days. A single positive screening test will accurately predict HIV infection in populations of moderate or high prevalence, however, there is a risk of false positive results in populations of low HIV prevalence. Institutions providing obstetrical deliveries should make an informed decision, based on local epidemiology, as to the potential benefit of implementing rapid screening during labor for women without HIV test results. In coming years, use of paired rapid tests (from different manufacturers) may prove to have sufficient predictive value to be useful in this setting throughout Michigan, regardless of local HIV prevalence.

For health care facilities without rapid testing, those facilities may want to consider implementing expedited HIV testing. In absence of both testing methods, health care providers need to make a decision regarding presumptive treatment for women that test only ELISA positive at delivery. (For further recommendations on presumptive treatment, please refer to page 42.)

Occasionally, women will decline to choose testing after HIV counseling has been provided. In such cases, it is important to ensure: 1) enough information about HIV and the test has been provided; 2) that it was provided in an understandable, believable, and supportive way; and 3) that no confusion has resulted about her options and the risks and benefits of antiretroviral therapy. This information should be communicated during routine obstetrical care to help patients make an informed decision about HIV testing. Some clinicians have found benefit in providing risk assessment and information about testing and waiting a period of time (the next visit or two) to allow women the opportunity to process the information before repeating the offer of testing. This is particularly helpful for patients who feel uncertainty in their decision-making.

Health care providers should ensure that every pregnant woman who is tested and found to be HIV-positive receive support and counseling. In addition, clinicians should provide women who choose to take antiretroviral or other therapies with the necessary care and support to ensure adherence to the regimen. Most importantly, women who are HIV positive must be referred to health care providers and organizations qualified to provide HIV specialty care to pregnant women, including but not limited to Ryan White CARE Act Title IV programs and community-based providers.

IMPORTANT CLINICAL CONSIDERATIONS

Clinical guidelines are dynamic and change frequently as new scientific insights allow clinicians to use different and frequently improved interventions to battle and control HIV infection. Health care providers may obtain timely information about current practice recommendations through the HIV/AIDS information website <http://www.aidsinfo.nih.gov>.

The combination of two laboratory results, the absolute (or percent) CD4+ lymphocyte count, and the quantitative measure of plasma HIV RNA (often called the viral load) provide much more prognostic information than either alone. A patient's level of plasma HIV RNA strongly indicates the expected rate of progression of his/her HIV disease: higher RNA levels correlate with more rapid progression. Quantitative plasma HIV RNA can be measured using one of three tests (RT-PCR known as Amplicor by Roche, bDNA by Chiron, and NucliSens by Organin Technika), but results should not be compared across methods. Further, because of variability in all of these tests, baseline values before treatment are best obtained by averaging two separate assays on two separate specimens drawn on different days. Since acute illnesses and vaccinations can transiently raise viral load, HIV RNA testing should be postponed several weeks following an illness or vaccination. A patient's CD4+ lymphocyte count indicates how far immune destruction has progressed. CD4+ cell counts of 500/ μ L or greater are generally considered normal, although the lower limit of normal varies by laboratory. A result of $<200/\mu$ L CD4+ cells is defined by the CDC as AIDS even in the absence of symptoms and should be reported to the Michigan Department of Community Health, HIV/AIDS Surveillance Section. (Lansing 517-335-8165, Detroit 313-876-0353.)

Information regarding the correlation of viral load with risk for perinatal transmission remains unclear. Though earlier studies revealed conflicting findings, antiretroviral therapy appears to decrease transmission regardless of maternal HIV-1 RNA level. However, transmission has been noted to occur over a broad range of viral load levels, including when HIV-1 RNA is not detectable. Therefore, antiretroviral chemoprophylaxis should be used in all pregnant women, regardless of the HIV-1 RNA levels. The goal of therapy should be to reduce the viral load to 1,000 copies or less.

The optimal time to initiate therapy in asymptomatic individuals with >200 CD4+ T cells is not known. This table provides general guidance rather than absolute recommendations for an individual patient. All decisions to initiate therapy should be based on prognosis as determined by the CD4+ T cell count and level of plasma HIV RNA, the potential benefits and risks of therapy, and the willingness of the patient to accept therapy. The table below adopted from the Guidelines for the Use of Antiretroviral Agents In HIV-1 Infected Adults and Adolescents provides a guide of when to initiate antiretroviral therapy. For specific treatment please consult the Guidelines online at www.nihinfo.org/guidelines or consult with a doctor specializing in HIV care.

* Clinical benefit has been demonstrated in controlled trials only for patients with CD4+ T cells $<200/\text{mm}^3$. However, most experts would offer therapy at a CD4+ T cell threshold $<350/\text{mm}^3$. A recent evaluation of data from the MACS cohort of 231 individuals with CD4+ T cell counts >200 and <350 cells/ mm^3 demonstrated that of 40 (17%) individuals with plasma HIV RNA $<10,000$ copies/mL, none progressed to AIDS by 3 years (Alvaro Munoz, personal communication). Of 28 individuals (29%) with plasma viremia of 10,000–20,000 copies/mL, 4% and 11% progressed to AIDS at 2 and 3 years respectively. Plasma HIV RNA was calculated as RT-PCR values from measured bDNA values.

Although there was a 2-2.5-fold difference between RT-PCR and the first bDNA assay (version 2.0), with the current bDNA assay (version 3.0), values obtained by bDNA and RT-PCR are similar except at the lower end of the linear range ($<1,500$ copies/mL).

INITIAL CARE OF THE PREGNANT HIV POSITIVE WOMAN

The initial evaluation of an HIV positive woman who is pregnant should include assessment of the status of her HIV disease, provision of information regarding initiating or changing treatments, and a review of the interventions available to help lower the risk of mother-to-child HIV transmission. Components of the initial assessment may include the following:

1. Laboratory tests to assess the current status of her HIV disease, such as blood studies to determine the viral load of HIV (quantity of RNA) and the number of CD4 or helper T cells, which are important for the individual's immune system. The woman's status influences the choice of treatments for her own care and the likelihood of HIV transmission during pregnancy or delivery.
2. Obtain a history of any prior or current antiretroviral therapy. This is important since drugs taken currently or in the past influence the current HIV viral load and CD4 cells, as well as the degree of sensitivity of the remaining virus to these types of drugs. In general, the decision regarding starting, continuing, or changing antiretroviral treatment regimens for pregnant women should be based on the same criteria used for non-pregnant individuals, except that the potential impact such medications may have on the developing fetus needs to be considered.
3. Medications taken (or ones that should be given) for prevention of opportunistic infections, such as *Pneumocystis carinii* pneumonia (PCP) or *Mycobacterium avium* complex (MAC) should be evaluated. In general, these medicines are usually given to patients with CD4 counts less than 200/ μ L. When it is felt such prophylaxis or treatment is necessary, the specific medications chosen may be influenced by the stage of pregnancy and concerns regarding the potentially harmful effects of certain drugs on the developing fetus.
4. Combination antiretroviral therapy using three antiretroviral drugs, also called highly active antiretroviral therapy or "HAART", is currently the standard for treatment of non-pregnant individuals and for pregnant women who require treatment as well. ZDV is included as a component of maternal HAART therapy if possible. Even if ZDV is not used during pregnancy, it is still recommended to give ZDV during labor to the mother and to the newborn for six weeks after birth.
5. A careful consideration of the potentially harmful (teratogenic) effects of certain antiretroviral medications on the growth and development of the fetus should occur early in the discussion with the patient. The fetus is most susceptible to potential teratogenic effects during the first 10 weeks of gestation.
6. Discussion of the important benefits of therapy with ZDV for the mother during pregnancy and labor and for the newborn for six weeks after birth. This treatment is based on the results of ACTG 076.

Appropriate support services and their importance for optimal maternal and infant health should be disclosed to the patient. Different patients will have different circumstances and needs: some HIV-infected women may require drug abuse treatment, mental health services, and/or other support services in coordination with appropriate prenatal, primary, and HIV specialty care. A discussion regarding long-term planning for the care of the child in the event of maternal illness is important.

FACTORS THAT INFLUENCE MOTHER TO CHILD TRANSMISSION

Multiple viral, immunologic, and physical factors may influence the transmission of HIV from a pregnant woman to her infant. Cigarette smoking, illicit drug use and unprotected sexual intercourse with multiple partners during pregnancy have been associated with increased risk for perinatal HIV-1 transmission. It is reasonable to suggest that cessation of these practices might reduce this risk. Of special importance is the CDC recommendation that HIV infected women in the United States refrain from breastfeeding to avoid postnatal transmission of HIV-1 to their infants through breast milk. Other important factors implicated in MTCT include duration of membrane rupture (greater than 4 hours), delivery of a previously infected child, and potentially risky obstetrical interventions (placement of scalp electrodes, fetal scalp pH sampling, amniocentesis, and percutaneous umbilical blood sampling.) Obstetrical workers should avoid performing procedures that could increase the risk of vertical transmission. Assisted rupture of the amniotic membranes removes a natural barrier between mother and fetus and is to be avoided. The avoidance of procedures such as amniocentesis and cordocentesis is based upon a theoretical risk that the introduction of a needle into the amniotic cavity that traverses the mother's abdomen and uterine wall will introduce maternal blood cells to the intrauterine cavity, thus increasing the risk for MTCT.

OVERVIEW OF THE ADMINISTRATION OF ANTIRETROVIRAL THERAPY IN PREGNANCY

ANTIRETROVIRAL DRUGS AND PREGNANCY

In the ACTG 076 trial, ZDV monotherapy was intended to decrease mother to child transmission of HIV and was not prescribed to stabilize the health of women with HIV infection. Now with the demonstration of the superiority of combination therapy (or highly active antiretroviral therapy, HAART) compared to antiretroviral monotherapy, ZDV therapy alone is now considered sub optimal for the treatment of HIV infection. Antiretroviral monotherapy should only be considered for pregnant women for whom combination antiretroviral therapy is not indicated or has been refused.

The Pediatric AIDS Clinical Trials Group 076 Zidovudine (ZDV) Regimen: (Adopted from the Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, June 16, 2003.

Throughout pregnancy, clinicians should evaluate women with HIV infection for clinical and immunologic disease progression and for the need for antiretroviral therapy for maternal indications. In women with advanced immunosuppression, antiretroviral therapy for maternal indications should be recommended after consultation with a physician skilled in AIDS medicine. Effective and durable HIV therapy maximally suppresses viral replication while sustaining immune function and reducing the development of resistance. Current guidelines for antiretroviral therapy balance the benefit of potent therapy with the risk of long-term side effects and the possible emergence of drug resistance. Use of antiretroviral therapy in pregnancy combines their use to improve the health of the woman with their use to reduce perinatal transmission.

Current treatment recommendations for HIV-1-infected pregnant women are based on the belief that therapies of accepted benefit to women should not be withheld during pregnancy unless there are documented adverse effects on the mother, fetus, or infant and these adverse effects outweigh the benefit to the woman. Since there is no compelling evidence of additional risk or data to support a therapeutic advantage to the use of an alternative therapy, the guidelines for optimal antiretroviral therapy in pregnant HIV-1-infected women should be the same as those delineated for non-pregnant adults. These complex regimens should be initiated and managed in consultation with clinicians experienced in HIV/AIDS care. Caregivers should not forget that the potential impact of optimal therapy on the fetus and infant is unknown. Long-term follow-up is needed for children who have exposure to antiretroviral drugs in utero. Therefore, any decision to use any antiretroviral drug during pregnancy should be made by the woman following discussion with her health care provider regarding the known and unknown benefits and risks to her and her fetus.

Potent combination therapy usually includes at least 3 medications: two from the class of nucleoside analogue reverse transcriptase inhibitors (NRTI) and one from either the non-nucleoside reverse transcriptase inhibitor class (NNRTI) or the protease inhibitor class (PI). However, some adjustments may be made during pregnancy, for example, avoidance of the teratogenic drugs efavirenz (Sustiva) and hydroxyurea (Hydrea). Certain combinations of three nucleoside analogues have been proven to be less potent and durable than combinations including an NNRTI or PI. When constructing an antiretroviral regimen for a HIV positive pregnant woman, please consult [The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, June 16, 2003](http://www.aidsinfo.nih.gov/guidelines) at <http://www.aidsinfo.nih.gov/guidelines>.

Passage of antiretroviral drugs into breast milk has been evaluated for only a few antiretroviral drugs. ZDV, 3TC, and Nevirapine can be detected in the breast milk of women, and ddI, d4T, Abacavir, Delavirdine, Indinavir, Ritonavir, Saquinavir and Amprenavir can be detected in the breast milk of lactating rats. Limited data are available regarding either the efficacy of antiretroviral therapy for the prevention of postnatal transmission of HIV-1 through breast milk or the toxicity of long-term antiretroviral exposure of the infant through breast milk. Women who must temporarily discontinue therapy because of pregnancy-related hyperemesis should not resume therapy until sufficient time has elapsed to ensure that the drugs will be tolerated. To reduce the potential for emergence of resistance, if therapy requires temporary discontinuation for any reason during pregnancy, all drugs should be stopped and reintroduced simultaneously.

Preliminary data suggest that pre-existing ZDV resistance among previously treated women is associated with reduced efficacy of the ACTG 076 regimen. Therefore, women who have received prior ZDV therapy should be considered for combination antiretroviral treatment. Some women may acquire ZDV resistance without prior treatment.

Information concerning the safety of antiretrovirals in the antepartum and intrapartum period and for initial treatment of exposed newborns is limited. Much of the information available to clinicians has been gathered through the diligent efforts of reporting by caregivers in non-research related settings. Data concerning antiretroviral therapy in pregnancy has been reported to the Antiretroviral Pregnancy Registry since 1989. Currently, there is information available concerning 20 different medications or formulations. Clinicians are strongly encouraged to report prenatal exposure of neonates to ART to the Antiretroviral Pregnancy Registry. (1-800-258-4263 or www.APRegistry.com) A supplement to the Public Health Service guidelines entitled, [Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy](#) is available at the website for HIV/AIDS information previously cited. There is sufficient information to give patients considering the use of ART timely information about the FDA pregnancy category classification and any notable observations of importance to the clinician and patient.

In cases where maternal HIV resistance to antiretroviral agent is suspected, it is unclear whether antiretroviral treatment will still reduce the risk of mother to child HIV transmission. Patients who are infected with antiretroviral-resistant viral strains are also likely to be infected with antiretroviral-sensitive strains. It is unknown whether antiretroviral-resistant strains are more likely or less likely to be transmitted. Consultation with an HIV specialist is important to ensure appropriate and adequate therapy. Please refer to Table 1 on page 51 for recommendations related to antiretroviral drug resistance and drug resistance testing for pregnant women with HIV infection.

It is possible that sub-therapeutic dosing of antiretroviral drugs are associated with enhanced likelihood for the development of drug resistance. Women who must temporarily discontinue therapy due to pregnancy-related hyperemesis should not reinstitute therapy until sufficient time has elapsed to ensure that the drugs will be tolerated. If therapy requires temporary discontinuation for any reason during pregnancy, all drugs should be stopped and reintroduced at the same time.

Past trials of other perinatal interventions (intravenous anti-HIV immunoglobulin (PACTG 185) and very short course nevirapine superimposed on other antiretroviral therapy (PACTG 316)) demonstrate the potent effect of combination antiretroviral therapy in reducing vertical transmission even though the specific randomized intervention was not effective. In PACTG 316, mother to child transmission rates under 2% were achieved with successful combination antiretroviral treatment during pregnancy combined with intrapartum intravenous ZDV for the mother and post-partum oral ZDV for 6 weeks to the newborn. Current standards recommend pregnant women take a standard combination of antiretroviral medications, generally including ZDV, to reduce perinatal transmission regardless of their need for therapy for their own health.

Women with very low plasma HIV RNA levels (<1000 copies/mL) and those who wish to minimize the exposure of their infants to antiretroviral medications may opt for ZDV monotherapy using the classical ACTG 076 regimen. However, the efficacy of ZDV monotherapy in reducing perinatal transmission may be reduced in women with pre-existing ZDV-resistant virus.

Among all currently licensed antiretrovirals, ZDV has the most complete currently available data regarding safety and efficacy during the intrapartum period and for initial treatment of exposed newborns. Therefore, intrapartum intravenous (IV) ZDV and newborn oral ZDV should be discussed and offered regardless of the mother's antiretroviral regimen. If possible, the mother's combination oral regimen (except oral ZDV) should be continued during the intrapartum, with concurrent intravenous ZDV. Stavudine and ZDV cannot be used together due to cross-inhibition. In cases where maternal HIV resistance to antiretroviral agent is suspected, consultation with an HIV specialist is important to ensure appropriate and adequate therapy.

Trials of short course regimens performed since the ACTG 076 study were less effective. However, short course regimens were more effective than no intervention, in reducing vertical transmission. These studies and other observational data provide a rationale for interventions among laboring women and their newborns when antiretrovirals were not used during the pregnancy.

Plasma HIV-1 RNA levels correlate with the risk of vertical transmission even among antiretroviral treated women. However, transmission has been observed across the entire range of HIV-1 RNA levels. Antiretroviral therapy decreases transmission regardless of maternal HIV-1 RNA level and transmission may occur when HIV-1 RNA is not detectable. Therefore, antiretroviral chemoprophylaxis should be used in all pregnant HIV positive women, regardless of the HIV-1 RNA levels.

TOLERANCE OF ANTIRETROVIRAL THERAPY DURING PREGNANCY

Information concerning the safety of drugs in pregnancy comes from many sources, including animal toxicity data, anecdotal experience, registry data and clinical trials. More is known about ZDV in pregnancy, and its effect on the fetus and newborn, than is known about other antiretroviral agents, because of formal studies and its long use in this setting. In the ACTG 076 trial, maternal ZDV therapy was well tolerated. In general, the side effects commonly observed with ZDV therapy in adult patients included headache and

gastrointestinal intolerance. The other more serious adverse experiences reported among ZDV users, such as anemia, hepatitis, and steatosis/lactic acidosis, were not seen. The long-term effects on maternal health following a short course of antepartum ZDV are unknown. With increasing duration of antiretroviral therapy, there is the potential for diminished antiretroviral efficacy and/or the potential for the emergence of antiretroviral-resistant viral strains. The occurrence of these problems following a short course of maternal antiretroviral therapy and the potential long-term impact on maternal health remains unknown.

Maternal tolerance of combination antiretroviral medications seems similar to their tolerance by non-pregnant women, with three exceptions. Hyperemesis of pregnancy may interact with the gastrointestinal symptoms of certain medications and make adherence difficult, especially during the first trimester. Further, there have been case reports of maternal deaths from a rare complication of antiretroviral therapy, lactic acidosis with hepatosteatorosis, among women taking the combination of stavudine (d4T, Zerit) and didanosine (ddl, Videx) as part of their therapy. This complication has been more frequently reported in women than men, although it is not known if pregnancy increases the risk. Nevertheless, the combination of stavudine and didanosine should be avoided during pregnancy if at all possible. Finally, protease inhibitor therapy has been associated with insulin resistance, glucose intolerance, and diabetes. Pregnancy itself is a risk for both transient and persistent abnormalities of glucose metabolism, therefore close monitoring of pregnant women on protease inhibitor-based combination therapy is advised. For a review of potential toxicities of all licensed antiretroviral drugs, see Table 2 on page 52.

BIRTH DEFECTS AND ANTIRETROVIRAL THERAPY

Birth defects have not occurred at an increased rate among infants exposed to antiretroviral medications; current data would have allowed the identification of a 2-fold increase in birth defects for most of the currently used medications. Efavirenz treatment of pregnant cynomolgus monkeys caused birth defects in some offspring and its use is contraindicated during human pregnancy.

Fetal/newborn therapy was also well tolerated in the ACTG 076 study. The only side effect observed during a median follow-up of 4.2 years was mild anemia at age 6 weeks that resolved at 12 weeks of age. A European study found a 2.6-fold increased risk of preterm births among women taking combination antiretroviral therapy, whereas this effect was not found in a study of nearly 1,500 US women. Another European study raised the possibility of mitochondrial toxicity among infants with perinatal exposure to combination antiretrovirals. Most of the nucleoside analogue reverse transcriptase inhibitors have potential to cause mitochondrial toxicity, including neuropathy, myopathy, cardiomyopathy, pancreatitis, hepatic steatosis, and lactic acidosis. The French reported that, among 1,700 HIV-uninfected infants exposed to combination antiretrovirals in utero, mitochondrial dysfunction caused two deaths, symptoms in three children, and laboratory abnormalities in another three. A United States review of more than 16,000 infants exposed to antiretrovirals did not uncover any such events. The ACTG 076 study cohort of ZDV-exposed infants, and other cohorts of infants exposed in utero to combination antiretroviral agents will be followed for several additional years to assess whether ZDV may affect neurodevelopment, other organ function, or the risk for neoplasia.

Long-term risks remain uncertain and may include unanticipated serious toxicities. Without such information, choices of drugs should be individualized in discussions with the woman about data collected from preclinical and clinical testing of the individual drugs. Antiretrovirals agents should be prescribed by, or in close consultation with, clinicians experienced with their use.

SCHEDULED CESAREAN DELIVERY FOR THE PREVENTION OF VERTICAL TRANSMISSION OF HIV INFECTION

Recent data from an international randomized trial and a meta-analysis of patient data from 15 prospective cohort studies (7,800 mother-child pairs) indicates that there is a significant relationship between the mode of delivery and vertical transmission of HIV. Though this data was collected prior to the use of HAART and utilizes no maternal viral load information, scheduled Cesarean delivery reduces the likelihood of vertical transmission of HIV compared with either unscheduled cesarean delivery or vaginal delivery, regardless of whether the patient used antiretroviral therapy. It remains unclear as to whether this intervention offers any benefit to women on HAART or to women with low or undetectable maternal viral loads. It is also clear that maternal morbidity is greater with a Cesarean delivery than with vaginal delivery. This is true in HIV negative women as well.

The American College of Obstetricians and Gynecologists recommend the following for HIV positive pregnant women:

1. Counseling of patients about the study data indicating that care with Zidovudine therapy and scheduled Cesarean delivery yields a transmission risk of approximately 2%. This risk is similar to that seen among women with viral loads of less than 1,000 copies per milliliter without use of scheduled Cesarean delivery.
2. Women with viral loads greater than 1,000 copies per milliliter in the weeks before anticipated delivery should be counseled regarding the potential benefit of scheduled Cesarean delivery to reduce vertical transmission risk further.
3. Antiretroviral chemotherapy should be administered according to currently accepted guidelines for adults.
4. Though the College usually recommends that scheduled Cesarean deliveries not occur before 39 completed weeks of gestation, 38 completed weeks is recommended in women with HIV infection to reduce the likelihood of onset of labor or rupture of membranes before delivery. Amniocentesis to determine fetal lung maturity should be avoided whenever possible.
5. For those patients receiving intrapartum ZDV, adequate levels of the drug in the blood should be achieved via IV infusion if treatment is begun 3 hours preoperatively using the dosing schedule recommended by the Centers for Disease Control and Prevention listed in this document.
6. In addition, obstetrical workers should avoid performing procedures that could increase the risk of vertical transmission. Assisted rupture of the amniotic membranes removes a natural barrier between the mother and fetus and is to be avoided. Risk for vertical transmission increases with the length of membrane rupture. Other procedures to be avoided include invasive diagnostic interventions such as amniocentesis and cordocentesis. There is a theoretical risk that the introduction of a needle into the amniotic cavity that also traverses the mother's abdomen and uterine wall will introduce maternal blood cells to the intrauterine cavity.

GUIDELINES FOR ANTIRETROVIRAL THERAPY FOR THE INTERUPTION OF MOTHER TO CHILD HIV TRANSMISSION IN PREGNANT WOMEN WITH HIV INFECTION

1. Women who are not currently receiving antiretroviral therapy.

Initial immunologic (CD4+lymphocyte count) and virologic (plasma HIV RNA level) assessment should be performed. The mother should consult with an experienced HIV clinician regarding use of combination antiretroviral therapy during pregnancy.

Whether therapy is initiated for the prevention of mother to child or for maternal medical indications, therapy should begin after 10-12 weeks gestation (after organogenesis is complete) due to lack of information on drug safety in the first trimester.

Combination antiretroviral treatment is recommended for the health of the mother following the usual indications and for antiretroviral treatment of other adults. Women with baseline plasma HIV RNA levels above 1,000 copies/mL should be offered combination antiretroviral therapy during pregnancy as well, using the regimens suggested for adults and adolescents, even if they do not fulfill current guidelines for initiating therapy for their own health. In either case, ZDV should be part of combination therapy, unless toxicity or pre-existing resistance precludes its use.

Regardless of the regimen prescribed during pregnancy, intravenous ZDV should be offered during labor and oral ZDV provided to the newborn for the first 6 weeks of life, following the ACTG 076 protocol.

2. Women on antiretroviral therapy for their own health who become pregnant.

Women should continue on antiretroviral therapy with co-management by their obstetrical provider and their HIV care provider. Consultation with an expert in treating HIV in pregnancy may be appropriate as well.

If the pregnancy is recognized during the first trimester, a temporary interruption in antiretroviral therapy can be considered to avoid exposure of the fetus to these medications during the period of organogenesis. The risks and benefits of such interruptions in therapy are not known, and the decision, made by the woman with her providers, should be individualized. If discontinued, therapy can be resumed at 10-12 weeks at gestation.

If the current regimen does not include ZDV, there should be consideration of including it or substituting it for a drug in the current regimen. Knowledge of prior drug exposure, known or probable drug resistance of the patient's HIV, and history of drug intolerance or toxicity should be considered in this decision. Some clinicians recommend use of another nucleoside analogue in the regimen for pregnant women with either intolerance or resistance to ZDV. Regardless of inclusion of ZDV in the maternal treatment regimen, intrapartum intravenous ZDV should be given to the mother and post-partum oral ZDV should be given to the newborn as per the ACTG 076 regimen.

The risks of antiretrovirals during pregnancy are better defined for some medications than others. One non-nucleoside reverse transcriptase inhibitor, efavirenz (Sustiva) caused a high rate of birth defects when tested in pregnant cynomolgus monkeys and should not be used in pregnancy. Thus, for safety reasons some modifications in the antiretroviral therapy regimen may be appropriate.

3. Women on antiretroviral therapy who have a plasma HIV RNA level > 1,000 copies/mL at 36 weeks gestation, and women who present at 36 weeks gestation or later without prior antiretroviral therapy.

Consideration of an elective Caesarean section prior to the onset of labor should be considered for women on antiretroviral therapy who have a plasma HIV RNA level > 1,000 copies/mL at 36 weeks gestation, and women who present at 36 weeks gestation or later without prior antiretroviral therapy. The risks to the mother and potential benefit to the newborn must be discussed with the patient by her obstetric and HIV clinicians. Women electing to have a Caesarean delivery should receive intravenous ZDV for 3 hours prior to and during the surgery. Women who do not choose surgical delivery should receive oral antiretroviral therapy during the remainder of their pregnancy and IV ZDV during labor. In either case, post-partum ZDV should be provided to the newborn.

4. Women in labor who have not received antiretroviral therapy during their pregnancy.

While not as effective as the entire 3-stage regimen, antiretroviral therapy during labor and post-partum may reduce the risk of transmission by about 50%.

Four regimens are available for consideration: (a) Intrapartum IV ZDV with oral ZDV for the newborn, as in the second and third components of the ACTG 076 regimen; (b) oral nevirapine (Viramune) 200mg for the mother at the onset of labor, and 2mg/kg of oral nevirapine to the newborn within 48-72 hours of birth; (c) combined ZDV and lamivudine (Epivir) [maternal treatment during labor ZDV 300 mg po q3h with lamivudine 150 mg po q12h; infant treatment ZDV 4 mg/kg q 12h and lamivudine 2 mg/kg po q 12h, both for 7 days]; or (d) the combination of intrapartum and postpartum ZDV per the 076 protocol (as in regimen a) with oral nevirapine (as in regimen b).

Whatever regimen is suggested, risks and benefits must be discussed with the woman in labor and her agreement obtained prior to drug administration.

5. Women in labor who had planned for an elective Caesarean section.

Intravenous ZDV should be administered. Women in early labor that is not expected to progress rapidly or with intact membranes may be offered surgical delivery after the loading dose of intravenous ZDV, although the benefit may be less than a surgical delivery offered prior to the onset of labor. Alternatives include allowing the woman to labor and deliver vaginally, or hastening labor with medications. Invasive instrumentation, such as fetal scalp monitoring or rupturing the membranes, should be avoided if possible. Post-partum, the infant should receive oral ZDV.

6. Women who present in labor with ruptured membranes.

Delivery should be accomplished within 4-6 hours maximum from the time of membrane rupture. If this is not possible vaginally, Cesarean section should be considered.

7. Infants born to mothers who did not receive antiretroviral therapy or prophylaxis during pregnancy or labor.

Provide oral ZDV to the infant as in the ACTG 076 regimen starting as soon as possible after birth. For treatment to be most effective neonatal ZDV should be administered within 12-24 hours of birth. Some clinicians provide combination antiretroviral therapy (usually Nevirapine) to the infant in this setting, especially if the mother is known or suspected to have ZDV resistant HIV. The risks and benefits of combination therapy in this circumstance are not well known.

The mother should be referred for evaluation of her own HIV disease as soon as practical.

See Tables 3 and 4 for a synopsis of clinical scenarios and recommendations as outlined in [The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to](#)

Reduce Perinatal HIV-1 Transmission in the United States, for the use of antiretroviral drugs to reduce perinatal HIV transmission during pregnancy and by mode of delivery.

IMPORTANT ELEMENTS TO INCLUDE IN A RISK/BENEFIT DISCUSSION OF ANTIRETROVIRAL THERAPY TO PREVENT MOTHER TO CHILD HIV TRANSMISSION

MATERNAL CONSIDERATIONS

1. Short-term risks and side effects of currently licensed antiretroviral medications in adults are well defined; and vary with the drug used. Initial side effects of antiretroviral therapy can include headache, nausea, anxiety and insomnia. Some persons develop pigmentation of skin and nails or changes in hair texture. Longer term and more serious toxicities may include anemia, leukopenia, pancreatitis, peripheral neuropathy, abnormalities of glucose metabolism, dyslipidemia, changes in body habitus due to lipodystrophy, and hepatic steatosis with lactic acidosis.
2. Long-term risks of use of antiretroviral therapy prescribed only during pregnancy are not well defined. Short-term use of ZDV monotherapy during pregnancy has not led to high rates of ZDV resistance in treated women. There are no formal data on the effects of short courses of combination antiretroviral therapy during pregnancy on disease progression, selection for drug resistant HIV, or on future use of antiretroviral treatment is anticipated. Little or no compromise of future antiretroviral treatment is anticipated for women who are adherent with properly prescribed and monitored antiretroviral therapy during pregnancy.
3. Women for whom antiretroviral therapy is indicated for their own health are likely to enjoy the same benefits of improved immunologic function, delayed onset of opportunistic diseases, and prolonged survival, as non-pregnant women receiving such treatment. They are likely to experience similar risks of drug toxicity, which vary with the specific combination prescribed. No maternal toxicity has been apparent in the small studies of combined ZDV with Lamivudine (Epivir) during pregnancy or single dose Nevirapine (Viramune) during labor.
4. Postpartum fever is higher among HIV-infected women undergoing elective Caesarean section (6-7%) than among HIV-infected women delivering vaginally. In some studies, there has been an increase in wound infection, endometritis and pneumonia among HIV positive women undergoing surgical delivery compared with vaginal delivery. In most studies, the complication rate of elective Caesarean section for HIV-infected women has been about the same as that for HIV negative women. In a few retrospective studies, there was a slight increase in infectious complications among HIV infected women undergoing urgent or emergency surgical delivery. These complications were more frequent among women with lower CD4 lymphocyte counts or clinically advanced HIV disease.

MATERNAL CONSIDERATIONS IN ABSENCE OF CONFIRMATORY HIV DIAGNOSTIC TESTING

For health care facilities that do not have rapid testing or expedited standard testing, MDCH encourages the implementation of one of these testing strategies to assist health care providers to make clinical decision regarding antiretroviral prophylactic treatment for the prevention of mother to child transmission as outlined in the recommendations from the Centers for Disease Control and Prevention and the American Academy of Pediatrics. Furthermore, MDCH encourages that care facilities to have policies in place for all test results to be returned expeditiously to the ordering physician for use in clinical decision making.

If a woman tests ELISA positive during labor and delivery in absence of a confirmatory Western Blot by expedited standard testing or reactive using rapid testing, MDCH encourages health care providers to discuss with the mother the risk benefit of presumptive antiretroviral prophylactic treatment for the prevention of mother to child transmission. The Centers for Disease Control and Prevention, November 9, 2001 Revised Guidelines for HIV Counseling, Testing, and Referral and Revised Recommendations for HIV Screening of Pregnant Women allow room for clinical decision making in regards to presumptive treatment. The Guidelines state: "However, necessary peripartum interventions to reduce the risk for perinatal transmission might need to be based on the preliminary results of rapid testing at labor and delivery. Decisions regarding use of antiretroviral drugs to prevent perinatal transmission among women who are repeatedly reactive on a single ELISA (MDCH recommendation) or rapid HIV test require clinical judgment regarding initiation of prophylactic treatment before results of a confirmatory test are available."

More recently, a committee opinion on the evaluation and treatment of the HIV-exposed infant from the American Academy of Pediatrics states: "Starting antiretroviral infant prophylaxis as soon as possible after birth (before 24 hours of age) is critical to prevent perinatal transmission. Therefore, if antiretroviral prophylaxis is given to an infant born to a mother with a positive EIA or rapid test result, it should be initiated pending results of her confirmatory test. The decision whether to start antiretroviral prophylaxis would take into consideration the positive predictive value of the screening test and the potential benefits and risks of the prophylactic agents."

Based on the above recommendations, MDCH advocates for health care providers to use their clinical judgment in absence of a confirmatory Western Blot and at a minimum begin antiretroviral infant prophylaxis treatment. Maternal intra-partum antiretroviral prophylaxis treatment should also be considered. If the health care provider, based on their clinical judgment, chooses not to start maternal or infant antiretroviral prophylaxis treatment because they do not have a confirmatory Western Blot, MDCH recommends that the health care facility have a procedure in place to notify the woman expeditiously of a positive confirmatory Western Blot result in order to begin the infant on antiretroviral prophylaxis treatment as soon as possible.

FETAL/NEWBORN CONSIDERATIONS

1. Combined antepartum, intrapartum, and postpartum ZDV monotherapy reduced mother to child transmission by 67%.
2. Combination antenatal retroviral therapy, leading to plasma HIV RNA levels in the mother of less than 1,000 copies/mL just prior to delivery, along with intrapartum and postpartum ZDV, led to transmission rates between 0% and 3% in four observational studies.
3. Among women receiving ZDV for perinatal prophylaxis, elective Caesarean section reduced the rate of transmission by 75%. This effect was present in a prospective randomized controlled study of planned Caesarean section versus planned vaginal delivery, and also in a meta-analysis of 15 observational studies of elective Caesarean section. The benefit was similar among women not taking antiretroviral therapy. However, there are no studies to provide information on the effect of surgical delivery on women with different plasma HIV RNA levels just prior to delivery. Elective Caesarean section is not recommended to women with viral loads of 1,000 copies/mL or less prior to delivery, because their risk of transmission is close to zero (see above) and there is unlikely to be a significant benefit of surgical delivery.
4. Some protection is provided by brief courses of peripartum antiretroviral treatment. In one observational study from the United States, IV ZDV during labor followed by neonatal oral ZDV reduced perinatal transmission by 62%. In one randomized study in South Africa, combined oral ZDV and Lamivudine (3TC) during labor and for one week to the newborn reduced transmission by 38%. In Uganda, a single dose of Nevirapine to the mother in labor and a single dose to the newborn reduced perinatal transmission by 47%.
5. Short term toxicity of ZDV in newborns in ACTG 076 was limited to transient anemia, which was maximal at the conclusion of the 6-week post partum treatment. Twelve weeks post-partum, the anemia had completely resolved.
6. Long-term effects to children exposed to combination antiretroviral therapy in utero are unknown. Nine year follow-up of children exposed to ZDV monotherapy during the ACTG 076 regimen has not demonstrated toxicity. Nevertheless, close follow up of children perinatally exposed to ZDV and other antiretroviral agents is important.
7. Toxicities of other antiretroviral agents have not been as well studied. There was no apparent toxicity to the newborn in a small study of one week combined ZDV/lamivudine and in a single post-partum dose of nevirapine. A United States registry of infants with in-utero and perinatal exposure to various antiretrovirals has not demonstrated any specific risk of birth defects or other toxicity. A European study of children exposed in-utero raised the possibility of nervous system and other toxicities based on drug-induced mitochondrial damage. A similar study in the US did not identify occurrences of such toxicity.
8. The unknown long term risks of these treatments must be weighed against the dramatic reduction in perinatal transmission of HIV, still an incurable infection shortening the life of those infected.
9. Elective Caesarean section scheduled at 38 weeks entails a small increased risk that the infant's lungs will be premature requiring artificial ventilation. This risk is balanced against the possibility of spontaneous onset of labor before 39 weeks, which otherwise is the usual time for elective Caesarean section.

RECOMMENDATIONS FOR MONITORING OF ANTIRETROVIRAL THERAPY

MATERNAL THERAPY

Co-management of HIV infected women and their exposed newborns by the obstetrical provider, pediatric provider, and clinicians experienced in HIV care is strongly recommended.

Women receiving antiretroviral therapy during pregnancy should have a baseline CBC with differential and liver and kidney function tests. These tests should be repeated after one month of therapy, and then every 1-3 months depending on the baseline levels, drug combination, and stage of pregnancy. Dose interruption (of all antiretrovirals) or drug substitution (of the single drug suspected of toxicity) should be considered for hemoglobin <8.5 g or an unexplained increase in AST or ALT three times above baseline. Dose reduction should never be used to manage toxicity of antiretroviral drugs.

Frequent visits early during therapy are important to assist women in achieving >95% adherence with their therapy, which maximizes the therapeutic effect and reduces the emergence of drug resistance. Persons who take only 80% of their medication have a 30% lower virologic response rate compared with those who take >95% of their doses. Supporting the behavior change needed for high level adherence and managing drug toxicity are crucial issues in the use of antiretroviral medications. Clinicians may find it helpful to have an established support system to assist with this process (i.e., local health department, community based organization).

Plasma HIV RNA and CD4 lymphocyte count should be measured once or twice prior to the onset of antiretroviral therapy. HIV RNA levels plasma should be measured after 4-8 weeks of therapy and every 3-4 months including at week 36 of gestation to assess response to therapy. CD4 lymphocyte counts can be measured with the viral load.

Many experts recommend the use of HIV resistance testing prior to initiating therapy in pregnant women. Women with pre-existing drug resistance, because of prior therapy or acquisition of drug resistant virus, may not achieve plasma HIV RNA levels below 1,000 copies/mL prior to delivery on a regimen prescribed empirically. In the absence of more information, resistance testing for HIV-1 infected pregnant women should be done for the same indications as for non-pregnant persons: those with acute infection; those who have virologic failure with persistently detectable HIV-1 RNA levels while receiving antenatal therapy, or sub-optimal viral suppression after initiation of antiretroviral therapy; or those with a high likelihood of having resistant virus based on community prevalence of resistant virus, known drug resistance in the woman's sex partner, or other source of infection. Interpretation of HIV resistance tests (genotype or phenotype) is rapidly evolving and expert guidance is suggested.

See Table 1 page 51, for recommendations related to antiretroviral drug resistance as outlined in [The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.](#)

Successful implementation of the recommendations presented in this document will require coordination of the health care services provided by all practitioners who deliver care to women and their newborns. Access to oral antiretroviral agents for pregnant women should be assured. Intravenous ZDV should be made available for immediate use in the obstetrical suite; oral and intravenous ZDV should be readily available in the newborn nursery and oral liquid ZDV in the delivery hospital outpatient pharmacy. Hospitals should develop written plans for coordinating services among labor and delivery, neonatology, and pediatric and pharmacy services to ensure that antiretroviral agents are available for patients according to the treatment regimen. The newborn will require 6 weeks of therapy after delivery. It is essential that, prior to discharge, the mother be educated in administration of therapy to the newborn and have the medication in hand. A prescription is not sufficient as many pharmacies do not carry liquid ZDV and the prescription may not be filled. Such planning should enhance compliance with the therapeutic regimen in the immediate postpartum period. Therapy given pre- and intra-partum should be documented in the infant's medical record. If there is reason to doubt the mother's ability or willingness to provide post-partum therapy to the infant, a social service consult should be obtained prior to discharge.

NEWBORN THERAPY

Infants born to HIV positive mothers will usually be provided ZDV for the first six weeks of life. This therapy must begin within 12-24 hours after birth and continue in an uninterrupted fashion. The prescription should be written and the family must be taught how to administer liquid medication reliably to a newborn and the supply of medication assured.

The guidelines for the administration of newborn therapy are below: (Adopted from the Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States, June 16, 2003.)

Oral administration of ZDV to the newborn (ZDV syrup at 2 mg/kg body weight/dose every six hours for the first six weeks of life, beginning at to 8-12 hours after birth.)

Intravenous dosage for full-term infants who cannot tolerate oral intake is 1.5 mg/kg body weight intravenously every six hours. ZDV dosing for infants <35 weeks gestation at birth is 1.5 mg/kg/dose intravenously, or 2.0 mg/kg/dose orally, every 12 hours, advancing to every 8 hours at 2 weeks of age if >30 weeks gestation at birth or at 4 weeks of age if <30 weeks gestation at birth.

The major short-term toxicity of neonatal ZDV is macrocytic anemia, which is maximal at 6 weeks, just when the therapy is concluding. Infants should be monitored with a hemoglobin level every 2-4 weeks during the therapy, and until the hemoglobin returns to expected values for age. Dose interruption should be considered if the anemia is severe, but dose modification is not recommended. There are no data on substituting other antiretrovirals during the newborn period if serious ZDV toxicity occurs.

There have been no reports of increased birth defects among ZDV exposed infants. In 6 years of follow-up following ZDV treatment in the ACTG 076 trial, there have been no toxicities noted. European researchers reported on the possible occurrence of nervous system and other toxicities among a small number of ZDV exposed infants that may have been due to mitochondrial drug toxicity. United States researchers have not identified any such toxicities among ZDV exposed infants to date. Tumors have occurred in ZDV exposed offspring in some animal models but not others, often at doses that far exceed the exposure of human infants during HIV prophylaxis. Nevertheless, thorough follow-up of ZDV exposed children is important.

Infants carry maternal anti-HIV antibody for up to 18 months, and therefore may remain seropositive without infection. An ELISA cannot diagnose HIV infection in an infant. PCR tests done at birth run the risk of contamination with maternal blood and are best avoided. HIV DNA PCR or HIV RNA PCR assays are recommended at first visit and at one, two, and four months of age to assess the child's HIV infection status. Two positive HIV PCR tests are considered confirmation of HIV infection in the newborn. Negative PCR tests done at birth, and at one and two months of life provide nearly complete assurance that the child is HIV negative. For completeness, HIV DNA PCR should be repeated at 4 months and standard HIV antibody testing at 18 months to confirm that the infant is not infected. HIV DNA PCR testing is available for free through the Michigan Department of Community Health (517-335-9453). HIV culture can also be used for diagnosis, but is more expensive, slower, and inconvenient.

Prophylaxis for *Pneumocystis Carinii* Pneumonia (PCP) should be instituted for all HIV-infected infants from one month to one year of age, regardless of CD4 cell counts. If there is any uncertainty regarding a perinatally exposed infant's HIV infection status at 4-6 weeks, prophylaxis should be started and can be discontinued later if the infant proves to be uninfected. The most effective agent for prophylaxis is cotrimoxazole (trimethoprim-sulfamethoxazole, (also known as Bactrim or Septra) dosed as 5 mg TMP and 25 mg SMX per kg daily, or twice a day on alternate days. PCP is rare in the first month of life, and sulfa therapy during that time carries a risk of kernicterus, so prophylaxis is not recommended in the immediate post natal period. PCP prophylaxis is usually deferred for the first 4-6 weeks of the infant's life.

If HIV infection is diagnosed, most experts provide immediate combination antiretroviral therapy along with appropriate opportunistic infection prophylaxis and a modified schedule of immunizations. NOTE: Live virus immunizations would not be given if the CD4 count were significantly suppressed and are not due until one year of age. Clinicians are encouraged to consult with, or refer infected infants to, experts in pediatric HIV disease who can provide the technological and psychosocial interventions the child and family require. To review the Centers of Disease Control and Prevention 2002 recommended immunization schedule for children and learn about recent changes to these vaccine guidelines, see www.cdc.gov/nip/recs/child-schedule.htm.

PROGRAM IMPLEMENTATION AND COORDINATION OF HEALTH CARE SERVICES

Providers initiating antiretroviral therapy in pregnant women for the reduction of mother to child HIV transmission should coordinate services required for the successful completion of antiretroviral therapy during pregnancy (as per the recommendations presented in this document), during the labor and delivery period, and during the newborn period. Providers of prenatal and maternal/fetal care should develop plans with neonatal/child health care providers to assure antiretroviral availability for the newborn. HIV-infected women should be offered referrals to community based support services, such as case management and support groups, to appropriate agencies if financial aid is needed (such as the Family Independence Agency), and to other services such as treatment for substance abuse or mental health services as appropriate. Local health departments and the MDCH AIDS Hotline (800-872-2437) can provide patients and clinicians with information regarding local AIDS service organizations and case management.

The long-term goal of this effort is the maintenance of healthy families. Reducing mother to child HIV transmission is the first step; however, maintaining the health of the parents and the functioning of the family are also necessary. Steps taken to make antiretroviral therapy successful during pregnancy do not guarantee successful post-partum care. Linkages for ongoing medical care and psychosocial support for all members of the family should be built during the pregnancy, when the mother is accessing services regularly.

CONCLUSION: SUMMARY of CLINICAL GUIDELINES for the ADMINISTRATION of ANTIRETROVIRAL THERAPY for the PREVENTION of MOTHER to CHILD HIV TRANSMISSION

1. Identification of Pregnant Women with HIV Infection

The majority of perinatal HIV transmission in Michigan occurs because either HIV testing was not performed during prenatal care or the information was not made available to other clinicians, including the labor and delivery facility. Improving the rate of voluntary testing and improving confidential communication of results among relevant providers are key to further reductions of perinatal HIV transmissions in our state.

All women's health care providers should provide HIV antibody testing for all pregnant women and all women considering pregnancy. Testing -should be done as early as possible during pregnancy.

When results of prenatal HIV testing are not available for a woman in labor, use of a rapid screening HIV antibody test may still allow diagnosis of the infected mother in time for intra-partum and post-partum chemoprophylaxis.

2. Documentation of Maternal HIV Antibody Status and/or Maternal HIV Therapies

During admission for labor and delivery, routine history taking should include ascertainment of HIV serostatus. For women with an unknown or undocumented HIV status, Michigan law requires the woman be offered HIV testing at the time of labor and delivery. For health care facilities without rapid testing or expedited standard HIV testing, for pregnant women with a positive ELISA, MDCH recommends health care providers use their clinical judgment and consider starting antiretroviral infant prophylaxis treatment and also consider maternal intra-partum antiretroviral prophylaxis treatment. For those women who are known to be HIV infected, a history of antiretroviral use should also be obtained.

3. Antiretroviral Therapy for the Interruption of Mother to Child HIV Transmission in Pregnant Women

All HIV positive pregnant women should be offered ART. In general, this will include a combination of three or more drugs. All HIV positive pregnant women should be offered combined antepartum, intrapartum, and newborn ZDV regimen as recommended per the ACTG 076 study protocol. For women with a viral load greater than 1,000 copies/mL, it is recommended that ZDV be part of potent combination antiretroviral therapy offered in consultation with an experienced HIV/AIDS clinician.

For women with HIV-related symptoms, CD4 cell counts < 350 cells/mm, and/or a viral load > 55,000 copies/mL, combination antiretroviral therapy should be offered for their own health in consultation with an experienced HIV/AIDS specialist. ZDV should be part of combination therapy during pregnancy. Intrapartum intravenous ZDV and oral newborn ZDV should be discussed and offered as well.

Women with plasma viral loads greater than 1,000 copies/mL at 36 weeks should be offered scheduled Cesarean-section with pre- and intra-operative intravenous ZDV, and postpartum ZDV for the infant.

Care should be taken to keep the membranes intact as long as possible and to deliver the infant within 4 hours of spontaneous rupture. However, membrane rupture beyond 4 hours is not an indication for Caesarean delivery.

For women in labor who have never received any antepartum maternal antiretroviral therapy (regardless of maternal CD4 cell count), an antiretroviral regimen combining intrapartum and newborn therapy should be discussed and offered.

Virologic, immunologic or clinical failure of antiretroviral therapy or intolerance of such therapy should be co-managed with an HIV-experienced clinician. Even if maternal therapy is discontinued, intrapartum and newborn therapy should be discussed and offered unless the maternal intolerance consists of a severe or life-threatening toxicity, such as anaphylaxis.

5. Program Implementation/Coordination of Health Care Services

Providers initiating antiretroviral therapy during pregnancy should coordinate services and social support, which may be required for the successful completion of combination therapy during the antenatal period, intravenous ZDV during the labor and delivery period, and oral ZDV during the newborn period. Providers of prenatal and maternal/fetal care should develop plans with neonatal/child health care providers to assure ZDV availability for the newborn.

6. Use of Consultants

Standards for HIV care, use of antiretrovirals, resistance testing, and interventions to reduce perinatal transmission are rapidly evolving. The material in this document is current at the time of writing, and reflects published US standards through July 2003. However, obstetrical and pediatric care providers who are not otherwise expert in HIV/AIDS care are encouraged to consult, formally or informally, with experts to maximize benefits to their patients.

Table 1: Recommendations Related to Antiretroviral Drug Resistance and Drug Resistance Testing for Pregnant Women with HIV Infection (Adopted from The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.) Based on 2003 PHS Guidelines. Please refer to 2004 Guidelines at http://www.aidsinfo.nih.gov/guidelines/perinatal/PER_062304.pdf

Table 2: Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy (Adopted from The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.) Based on 2003 PHS Guidelines. Please refer to 2004 Guidelines at http://www.aidsinfo.nih.gov/guidelines/perinatal/PER_062304.pdf

Preclinical and Clinical Data Relevant to the Use of Antiretrovirals in Pregnancy

Table 3: Clinical Scenarios and Recommendations for the Use of Antiretroviral Drugs to Reduce Perinatal Human Immunodeficiency Virus Type 1 (HIV-1) Transmission (Adopted from The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.) Based on 2003 PHS Guidelines. Please refer to 2004 Guidelines at http://www.aidsinfo.nih.gov/guidelines/perinatal/PER_062304.pdf

Table 4: Clinical Situation and Recommendation Regarding Mode of Delivery to Reduce Perinatal Human Immunodeficiency Virus Type 1 (HIV-1) Transmission (Adopted from The United States Public Health Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.) Based on 2003 PHS Guidelines. Please refer to 2004 Guidelines at http://www.aidsinfo.nih.gov/guidelines/perinatal/PER_062304.pdf

TELEPHONE NUMBERS AND REFERENCES:

HIV/AIDS Treatment Information Services, PHS 1-800-HIV-0440 or <http://www.aidsinfo.nih.gov>

Perinatal Hotline

1-888-448-8765

Referral Service 24 hours a day/7 days a week

National Perinatal HIV Consultation and

Warmline

National HIV Telephone Consultation Service

1-800-933-3413

Monday-Friday 8am-8pm EST

Voicemail 24 hours a day/7 days a week

Obstetric/Gynecology Information

Arthur James, MD, Borgess Medical Center (Kalamazoo) 269-226-7000
Theodore Jones, MD, WSU/DMC (Detroit) 313-745-4380*
313-993-3400*
313-745-0203 pager 2789#
Laura Zuidema, MD, West Michigan Perinatal Center 616-391-3681
(Grand Rapids)
**Daytime clinic number and night/weekend answering service number*

Infectious Diseases

Jonathan Cohn, MD, WSU/DMC (Detroit) 313-745-9035*
Charles Craig, MD, (Ann Arbor) 734-434-4333
Del DeHart, MD (Saginaw) 517-860-4735
David Dobbie, MD, McAuley Health Center (Grand Rapids) 616-913-8200
Thomas Flynn, MD, Bronson Methodist Hospital (Kalamazoo) 269-341-6400
H. Gunner-Deery, MD, (Petoskey) 616-487-6590
Peter Gulick, DO, MSU College of Osteopathic Medicine 517-377-8638
Mark Harrison, MD, South Western Medical Clinic, 269-471-1496
(Berrien Center)
Daniel Kaul, MD, University of Michigan (Ann Arbor) 734-936-8186
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William Lo, MD, McLaren Hospital Clinic (Flint) 810-342-2000
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Microbiology/Pediatrics Michigan State University

Family Practice

Susan Schooley, MD, Henry Ford Health Systems 313-874-5379

HIV/AIDS RELATED HOTLINES AND/OR WEBSITES

NATIONAL

NAME	HOTLINE	WEB SITE
AIDS Clinical Trials Service	800-TRIALS-A	http://www.aidsinfo.nih.gov
AIDS Hotline	800-872-AIDS	http://www.aidspartnership.org
AIDS Hotline (TDD)	800-332-0849	
AIDS Medicines in Development	202-835-3450	http://www.phrma.org
AIDS National Interfaith Network	202-842-0010	http://aidsinterfaithnetwork.org

AIDS/HIV Treatment Directory	800-39-AMFAR	http://www.amfar.org/globalink
Association of Nurses in AIDS Care	800-260-6780	http://anacnet.org
Centers for Disease Control and Prevention	404-639-3311	http://www.cdc.gov
HIV/AIDS Resources of the World Wide Web		http://www.themeasurementgroup.com/hiv_info.htm
Human Resources Services Administration - HRSA	888-275-4772	http://hrsa.gov
SAMHSA - Substance Abuse and Mental Health Services Administration		http://www.findtreatment.samhsa.gov
State by State Listing of AIDS Organizations		http://hardtruth.gti.net/State%20HIV-AIDS%20Organizations.htm
United States HIV/AIDS Service Organizations		http://www.thebody.com/hotlines/other.html
USPHS Guidelines on Use of Antiretrovirals in Pregnant Women Infected with HIV-1 for Maternal Health & Reducing Perinatal HIV-1 Transmission-2004		http://www.aidsinfo.nih.gov/guidelines/perinatal/PER062304.pdf

HIV/AIDS RELATED HOTLINES AND/OR WEBSITES

STATE

NAME	HOTLINE	WEB SITE
AIDS Partnership Michigan	800-872-2437	http://aidspartnership.org
AIDS Drug Assistance Program	800-826-6565	http://www.michigan.gov/mdch
Community AIDS Resource & Education Service of SW Michigan	800-944-2437	http://www.caresswm.org/cares2b.html
Detroit Community AIDS Library		http://www.detroit.lib.mi.us/dcal
Detroit Department of Health and Wellness Promotion	313-833-1450	http://www.ci.detroit.mi.us/health_hiv/RESPONSE.htm
HIV Care Services	212-343-8200	http://www.hivcs.org/links.html
HIV/AIDS Resource Center	800-578-2300	http://www.r2harc.org
HIV/AIDS Resource Network	800-578-2300	http://comnet.org/local/orgs/harc/res_links.html
Inter-Tribe Council of Michigan	800-562-4957	http://www.itcmi.org/hivhealthcare.html
Jackson County HIV/AIDS Awareness Coalition Resources		http://webspawner.com/users/jaanresources/
Michigan Department of	517-241-5900	http://www.michigan.gov/mdch

Community Health (MDCH)
Division of Health, Wellness and
Disease Control
Drug Assistance Program

Midwest AIDS Training and Education Center (MATEC)	313-962-4040	http://www.uic.edu/depts/matec/
MDCH Health Electronic Library		http://www.mchel.org/government.html
MDCH HIV/AIDS Hotline	800-872-2437	
Michigan HIV News (MDCH)		http://www.mihivnews.com/resource.htm
PWH/A Support and Referral Hotline	800-350PWAS	http://www.friendsalliance.org
Women, Infant, Children and Families	800-26BIRTH	HTTP://WWW.MICHIGAN.GOV/MDCH

All pregnant HIV-1-infected women should be offered highly active antiretroviral therapy to maximally suppress viral replication, reduce the risk of perinatal transmission, and minimize the risk of development of resistant virus.

For women for whom combination antiretroviral therapy would be considered optional (HIV-1 RNA < 1,000 copies/mL) and who wish to restrict their exposure to antiretroviral drugs during pregnancy, monotherapy with the three-part zidovudine (ZDV) prophylaxis regimen (or in selected circumstances, dual nucleosides) should be offered. In these circumstances, the development of resistance should be minimized by limited viral replication (assuming HIV-1 RNA levels remain low) and the time-limited exposure to ZDV. Monotherapy with ZDV does not suppress HIV-1 replication to undetectable levels in most cases. Theoretically, such therapy might select for ZDV-resistant viral variants, potentially limiting future treatment options. These considerations should be discussed with the pregnant woman.

Recommendation for resistance testing for HIV-1-infected pregnant women are the same as for non-pregnant patients: acute HIV-1 infection, virologic failure, sub-optimal viral suppression after initiation of antiretroviral therapy, or high likelihood of exposure to resistant virus based on community prevalence or source characteristics.

Women who have a history of presumed or documented ZDV resistance and are on antiretroviral regimens that do not include ZDV for their own health should still receive intravenous ZDV intrapartum and oral ZDV for their infants according to the PACTG 076 protocol whenever possible. A key mechanism by which ZDV reduces perinatal transmission is likely through pre- and post-exposure prophylaxis of the infant, which may be less dependent on drug sensitivity than is reduction of viral replication. However, these women are not good candidates for ZDV alone.

Optimal antiretroviral prophylaxis of the infant born to a woman with HIV-1 known to be resistant to ZDV or other agents should be determined in consultation with pediatric infectious disease specialists, taking into account resistance patterns, available drug formulations, and infant pharmacokinetic data, when available.

If women receiving combination therapy require temporary discontinuation for any reason during pregnancy, all drugs should be stopped and reintroduced simultaneously to reduce the potential for emergence of resistance.

Optimal adherence to antiretroviral medications is a key part of the strategy to reduce the development of resistance.

Because the prevalence of drug-resistant virus is an evolving phenomenon, surveillance is needed to monitor the prevalence of drug-resistant virus in pregnant women over time and the risk of transmission of resistant viral strains.

SCENARIO #1

HIV-1-infected pregnant women who have not received prior antiretroviral therapy.

- n Pregnant women with HIV-1 infection must receive standard clinical, immunologic, and virologic evaluation. Recommendations for initiation and choice of antiretroviral therapy should be based on the same parameters used for persons who are not pregnant, although the known and unknown risks and benefits of such therapy during pregnancy must be considered and discussed.
- n The three-part ZDV chemoprophylaxis regimen, initiated after the first trimester, should be recommended for all pregnant women with HIV-1 infection regardless of antenatal HIV RNA copy number to reduce the risk for perinatal transmission.

- n The combination of ZDV chemoprophylaxis with additional antiretroviral drugs for treatment of HIV-1 infection is recommended for infected women whose clinical, immunologic or virologic status requires treatment or who have HIV-1 RNA over 1,000 copies/mL regardless of clinical or immunologic status.
- n Women who are in the first trimester of pregnancy may consider delaying initiation of therapy until after 10-12 weeks' gestation.

SCENARIO #2

HIV-1-infected women receiving antiretroviral therapy during the current pregnancy.

- n HIV-1 infected women receiving antiretroviral therapy in whom pregnancy is identified after the first trimester should continue therapy. ZDV should be a component of the antenatal antiretroviral treatment regimen after the first trimester whenever possible, although this may not always be feasible.
- n For women receiving antiretroviral therapy in whom pregnancy is recognized during the first trimester, the woman should be counseled regarding the benefits and potential risks of antiretroviral administration during this period, and continuation of therapy should be considered. If therapy is discontinued during the first trimester, all drugs should be stopped and reintroduced simultaneously to avoid the development of drug resistance.
- n Regardless of the antepartum antiretroviral regimen, ZDV administration is recommended during the intrapartum period and for the newborn.

SCENARIO #3

HIV-1-infected women in labor who have had no prior therapy.

- n Several effective regimens are available (Table 4). These include:
 1. Intrapartum intravenous ZDV followed by six weeks of ZDV for the newborn;
 2. Oral ZDV and 3TC during labor, followed by one week of oral ZDV-3TC for the newborn;
 3. A single dose nevirapine at the onset of labor followed by a single dose of nevirapine for the newborn at age 48 hours, and
 4. The two-dose nevirapine regimen combined with intrapartum intravenous ZDV and six week ZDV for the newborn.
- n In the immediate postpartum period, the woman should have appropriate assessments (e.g., CD4⁺ count and HIV-1 RNA copy number) to determine whether antiretroviral therapy is recommended for her own health.

SCENARIO #4

Infants born to mothers who have received no antiretroviral therapy during pregnancy or intrapartum.

- n The six-week neonatal ZDV component of the ZDV chemoprophylactic regimen should be discussed with the mother and offered for the newborn.
- n ZDV should be initiated as soon as possible after delivery - preferably within 6-12 hours of birth.
- n Some clinicians may choose to use ZDV in combination with other antiretroviral drugs, particularly if the mother is known or suspected to have ZDV-resistant virus. However, the efficacy of this approach for prevention of transmission is unknown, and appropriate dosing regimens for neonates are incompletely defined.
- n In the immediate postpartum period, the woman should undergo appropriate assessments (e.g., CD4⁺ count and HIV-1 RNA copy number) to determine if antiretroviral therapy is required for her own health. The infant should undergo early diagnostic testing so that if HIV-infected, treatment can be initiated as soon as possible.

Note: Discussion of treatment options and recommendations should be noncoercive, and the final decision regarding the use of antiretroviral drugs is the responsibility of the woman. A decision to not accept treatment with ZDV or other drugs should not result in punitive action or denial of care. Use of ZDV should not be denied to a woman who wishes to minimize exposure of the fetus to other antiretroviral drugs and who therefore choose to receive only ZDV during pregnancy to reduce the risk for perinatal transmissions.

Scenario A

HIV-1-infected women presenting in late pregnancy (after about 36 weeks of gestation), known to be HIV-1-infected but not receiving antiretroviral therapy, and who have HIV-1 RNA level and lymphocyte subsets pending but unlikely to be available before delivery.

Therapy options should be discussed in detail. The woman should be started on antiretroviral therapy including at least the PACTG 076 ZDV regimen. The woman should be consulted that scheduled cesarean section is likely to reduce the risks of transmission to her infant. She should also be informed of the increased risks to her of cesarean section, including increased rates of postoperative infection, anesthesia risks, and other surgical risks.

If cesarean section is chosen, the procedure should be scheduled at 38 weeks of gestation based on the best available clinical information. When scheduled cesarean section is performed, the woman should receive continuous intravenous ZDV infusion beginning three hours before surgery and her infant should receive six weeks of ZDV therapy after birth. Options for continuing or initiating combination antiretroviral therapy after delivery should be discussed with the woman as soon as her viral load and lymphocyte subset results are available.

Scenario B

HIV-1-infected women who initiated prenatal care early in the third trimester, are receiving highly active combination antiretroviral therapy, and have an initial virologic response, but have HIV-1 RNA levels that remain substantially over 1,000 copies/mL at 36 weeks of gestation.

The current combination antiretroviral regimen should be continued as the HIV-1 RNA level is dropping appropriately. The woman should be counseled that although she is responding to the antiretroviral therapy, it is unlikely that her HIV-1 RNA level will fall below 1,000 copies/mL before delivery. Therefore, scheduled cesarean section may provide additional benefit in preventing intrapartum transmission of HIV-1. She should also be informed of the increased risks to her of cesarean section, including increased rates of postoperative infection, anesthesia risks, and surgical risks.

If she chooses scheduled cesarean section, it should be performed at 38 weeks' gestation according to the best available dating parameters, and intravenous ZDV should be begun at least three hours before surgery. Other antiretroviral medications should be continued on schedule as much as possible before and after surgery. The infant should receive oral ZDV for six weeks after birth. The importance of adhering to therapy after delivery for her own health should be emphasized.

Scenario C

HIV-1-infected women on highly active combination antiretroviral therapy with undetectable HIV-1 RNA level at 36 weeks of gestation.

The woman should be counseled that her risk of perinatal transmission of HIV-1 with a persistently undetectable HIV-1 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.

Cesarean section has an increased risk of complications for the woman compared to vaginal delivery, and these risks must be balanced against the uncertain benefit of cesarean section in this case.

Scenario D

HIV-1-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.

If labor is progressing rapidly, the woman should be allowed to deliver vaginally. 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.

If the woman is allowed to labor, scalp electrodes and other invasive monitoring and operative delivery should be avoided if possible. The infant should be treated with six weeks of ZDV therapy after birth.

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