



AIDS Line

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Perinatal HIV Prevention and the 2007 New Jersey Legislation2

C. Burr, S. Paul, L. Dimasi, and R. Fry

Cases.....8

P. Kloser and National Perinatal HIV Hotline



Metabolic Complications Associated with the Treatment of HIV-Infected Patients.....19

M. Fussa and S Paul

Cases.....8

P. Kloser and D. Mohammed



News Features

Updated Guidelines

Re: HIV & TB27

Treatment Interactions.....29

FDA Drug Cautions30

CDC HIV/AIDS Web Series30

Resources

Treatment Information

and Training Resources.....35

Save the Dates

October 14, 2008
Reducing Mother-to-Child
HIV Transmission in NJ
 (see page 16)

December 10, 2008
19th Annual HIV Medical Update
 Cherry Hill, NJ
 (see back page)

New Jersey's New Legislation for HIV Testing of Pregnant Women and Newborns

Sindy M. Paul, MD, MPD, FACPM and Linda Dimasi, MPA

As one of the first states with a high proportion of HIV/AIDS cases among women, New Jersey pioneered the first database to monitor perinatal exposure and transmission rates. New Jersey's enhanced perinatal surveillance includes a comprehensive review and abstraction of actual prenatal records, labor, and delivery records, and newborn pediatric records. Together with data from matched HIV/AIDS registry and birth files, the New Jersey Department of Health and Senior Services (NJDHSS), Division of HIV/AIDS Services (DHAS) can gather outcome indicator information to evaluate compliance with prevention guidelines, identify missed opportunities for prevention, and monitor the rate of perinatal transmission in New Jersey.



Beginning in 1992 all cases of children born to mothers who are HIV positive have been reportable to the NJDHSS (NJAC8:57-4.3). Any medical practitioner delivering or providing care to a child known to be perinatally exposed to HIV, or ordering a test resulting in the diagnosis of perinatally exposed HIV, shall, within 24 hours of receipt of a laboratory report indicating such a condition, report in writing such condition directly to the NJDHSS, DHAS on forms supplied by the NJDHSS, DHAS. For assistance with the reporting of perinatal exposures, or to request reporting forms, please call (609) 984-5940.

As indicated through the enhanced New Jersey perinatal surveillance system, children exposed to and infected with HIV through mother-to-child transmission have been reported in every county. Of the 1,335 pediatric HIV/AIDS cases reported to date, 93.5% are the result of vertical HIV transmission. Efforts to minimize the risk of vertical HIV transmission have resulted in a marked decrease in perinatal HIV transmission from 94 children (24.5%) in 1992 to two children (1.4%) in 2006. The major missed opportunity for the prevention of mother-to-child HIV transmission in New Jersey is women who present in labor with unknown HIV status.

The Centers for Disease Control and Prevention (CDC) published recommendations for opt-out HIV testing of pregnant women in first and third trimesters in September 2006.¹ In addition, the CDC recommends that women who present in labor with unknown HIV status should be offered opt-out rapid HIV testing.²

On December 26, 2007, Acting Governor Codey signed into law Assembly Bill No. 4218, which is identical to Senate Bill No. 2704. This law requires healthcare providers to test pregnant women for HIV as part of the routine prenatal care unless the woman refuses testing, and requires testing of certain newborns for HIV.

(Continued on page 36)

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CONTINUING EDUCATION INFORMATION

Perinatal HIV Prevention and the 2007 New Jersey Legislation

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Target Audience

This activity is designed for physicians and nurses, and for other health care professionals in New Jersey who are involved in the care of women of childbearing age and/or persons with HIV/AIDS.

Statement of Need

On November 2, 2007, the CDC issued *Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*: <http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf>

New legislation takes effect in New Jersey in June 2008 (P.L. 2007 C218) which will have a significant effect both on providers caring for pregnant women and on the women in care. Medical management of pregnant women and pregnant women with HIV infection is rapidly evolving. These legal and medical management issues pose a challenge as clinicians must keep up-to-date. This article will discuss the practical impact of the new law on delivery of care to pregnant women and will highlight recent changes in clinical management.

Learning Objectives

Upon the completion of this activity, participants should be able to:

1. Distinguish between routine and opt-out HIV testing protocols.
2. Outline the required information to provide to pregnant women before administering HIV tests under the 2007 New Jersey legislation.
3. Explain the increased emphasis on HIV testing in the third-trimester or at labor and delivery.
4. Summarize the interventions with HIV-positive women which can reduce perinatal transmission, from pre-conceptual counseling through post-delivery.

Method of Instruction

Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the post-test which consists of a series of multiple-choice and True/False questions.

Upon completing this activity as designed and achieving a passing score of 70% or more on the post-test, participants will receive a credit letter and the test answer key four (4) weeks after receipt of the post-test, registration, and evaluation materials. Estimated time to complete this activity as designed is 1.25 hours.

Accreditation

Physicians: UMDNJ-Center for Continuing & Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UMDNJ-Center for Continuing & Outreach Education designates this educational activity for a maximum of 1.25 Category 1 AMA PRA Credit(s)[™]. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Nurses: The University of Medicine & Dentistry of New Jersey-Center for Continuing & Outreach Education is an approved provider of continuing nursing education by NJSNA, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is awarded 1.25 contact hours (60 minute CH).

Provider approved by the California Board of Registered Nursing, Provider Number CEP 13780.

General: UMDNJ-Center for Continuing & Outreach Education certifies that this program meets the criteria for up to 0.125 Continuing Education Units (CEUs), provided the activity is completed as designed. One CEU equals 10 contact hours of participation in an organized continuing education experience under responsible sponsorship, capable direction and qualified instruction.

Review: This activity was peer reviewed for relevance, accuracy of content, and balance of presentation by Patricia Kloser, MD, MPH; and Brenda Christian, MEd, PA-C; and pilot tested for relevance and time required for participation by Kinshasa Morton, MD; Bonnie Abedini, RN, MSN; Linda Berezny, RN, BA; and Mary C. Krug, RN, MSN, APN-C.

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Faculty Disclosure Declarations

The following have no financial relationships to disclose: faculty: Carolyn Burr, EdD, RN; Sindy M. Paul, MD, MPH, FACPM; Linda Dimasi, MPA; and Rebecca Fry, MSN, APN; and reviewers: Patricia Kloser, MD, MPH; Brenda Christian, MEd, PA-C; Kinshasa Morton, MD; Bonnie Abedini, BSN, MS; Linda Berezny, RN, BA; and Mary C. Krug, RN, MSN, APN-C; and *New Jersey AIDSLine* editor Kimi Nakata, MSW, MPH.

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This activity does not contain information of commercial products/devices that are unlabeled for use or investigational uses of products not yet approved.

Disclaimer

The views expressed in this activity are those of the faculty. It should not be inferred or assumed that they are expressing the views of NJDHSS-Division of HIV/AIDS Services, UMDNJ, or any manufacturer of pharmaceuticals. The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult the full prescribing information on any agent(s) presented in this activity for recommended dosage, indications, contraindications, warnings, precautions, and adverse effects before prescribing any medication. This is particularly important when a drug is new or infrequently prescribed.

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Perinatal HIV Prevention and the 2007 New Jersey Legislation

Carolyn Burr EdD, RN; Sindy M. Paul, MD, MPD, FACPM; Linda Dimasi, MPA; and Rebecca Fry, MSN, APN

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

1. Distinguish between routine and opt-out HIV testing protocols.
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INTRODUCTION

Reducing the risk of perinatal HIV transmission is a public health priority in New Jersey. The risk of vertical HIV transmission without appropriate obstetrical care is 25%. With prenatal education and testing, antiretroviral agents starting in the second trimester, and an elective caesarian section at 38 weeks gestational age if the viral load is greater than 1,000, the risk of transmission can be reduced to 1%-2%.¹

Children exposed to and infected with HIV through mother-to-child transmission have been reported in every county in New Jersey. Of the 1,335 pediatric HIV/AIDS cases reported to date, 93.5% are the result of vertical HIV transmission. An ongoing concerted effort to minimize the risk of vertical transmission in New Jersey has been successful. Perinatal HIV transmission has decreased from 94 children (24.5%) in 1992 to two children (1.4%) in 2006.

Continued success in preventing HIV transmission from mother-to-child depends on knowing the mother's HIV status through HIV testing as part of routine prenatal care, proper obstetrical care, and pediatric care of the newborn.

(Continued on next page)

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To obtain continuing education credit for this activity, read the article and complete the quiz, registration and evaluation forms that follow.



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HIV Counseling and Testing of Pregnant Women and Newborns

The most recent Centers for Disease Control and Prevention (CDC) recommendations for HIV testing of pregnant women include opt-out testing of pregnant women in the first and third trimesters as part of routine prenatal care.² In addition, CDC recommends that women who present in labor with unknown HIV status should be offered opt-out rapid HIV testing. CDC recommends postpartum, rapid testing of the newborn as soon as possible after birth if the mother's HIV status is unknown.³

New legislation takes effect in New Jersey in June 2008 (P.L. 2007 C218) which will have a significant effect both on providers caring for pregnant women and on the women in care. Medical management of pregnant women and pregnant women with HIV infection is rapidly evolving. These legal and medical management issues pose a challenge as clinicians must keep up-to-date. This article will discuss the practical impact of the new law on delivery of care to pregnant women and will highlight recent changes in clinical management.

While routine offering of HIV testing to pregnant women has been the New Jersey law for many years, the new legislation, which goes into effect June 30, 2008, states that HIV testing should be included in routine prenatal testing using an "opt-out" approach. With the "opt-out" approach, the HIV test will be done routinely along with the standard battery of prenatal blood tests, unless the woman declines. The provider must give the patient information about HIV/AIDS, the benefits of testing for her and her baby, the available medical treatment for her, and interventions which reduce the infant's risk of HIV infection.

This approach to testing does not make any assumptions about behavior that could have increased a pregnant woman's risk for HIV. It only assumes that she has had unprotected

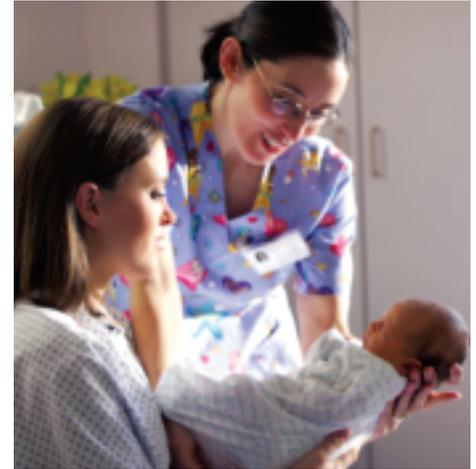
sex (in order to get pregnant) and could be at risk for HIV. For clinicians who have been routinely offering HIV testing to pregnant women, the legislation will not mean a major change.

A separate written informed consent is no longer required, but if a woman declines the routine HIV test, it should be noted in the medical record.

The legislation tries to assure that women know they are being tested for HIV by specifying the information they should be given. However, it leaves open to the clinician the options of how to deliver the information. It must be provided either orally, in person or, presumably, by video; or in writing through a pamphlet; and the woman must be offered an opportunity to ask questions. *If clinicians have not previously made HIV information available, they will need to decide when and how the HIV information is given to their patients.*

Some written support materials that would meet the standard set in the legislation currently are available to clinicians.

The American College of Obstetricians and Gynecologists (ACOG) has a small tear-off pad which details a number of the prenatal tests including HIV (ACOG, 2007, "HIV and Other Important Pregnancy Tests"). The ACOG tear pads are available in Spanish, French, Russian, and Chinese as well as English.



The *One Test. Two Lives.* campaign from the Centers for Disease Control and Prevention (CDC) also includes patient handouts discussing prenatal tests including HIV (CDC, *One Test. Two Lives.* and "Helpful Tests," available at www.cdcnpin.org).

Materials can be ordered from ACOG (www.ACOG.org or 800-762-2264) or requested free of charge from the National Prevention Information Network (NPIN). The *One Test. Two Lives.* materials also include a handout that describes how a clinician can respond if a patient is unsure about HIV testing.

The François-Xavier Bagnoud Center at UMDNJ has also developed a "script" for providers that offers suggestions for information sharing in prenatal settings (available in summer 2008 at www.fxbcenter.org). The New Jersey Department of Health and Senior Services (NJDHHS) is developing guidelines based on the legislation for information that needs to be given to pregnant women about HIV testing.

An ongoing concerted effort
to minimize the risk of vertical transmission in New Jersey
HAS BEEN SUCCESSFUL.

Perinatal HIV transmission has decreased from
94 children (24.5%) in 1992 to two children (1.4%) in 2006.



ONE TEST. TWO LIVES. CAMPAIGN:

The *One Test. Two Lives.* campaign from the Centers for Disease Control and Prevention (CDC) gives obstetric providers new tools to help ensure all patients get tested for HIV early in their pregnancy.

Perinatal transmission accounts for 91% of all AIDS cases among children in the United States. Antiretroviral therapy during pregnancy can reduce the transmission rate to 2% or less. The transmission rate is 25% without treatment.

One Test. Two Lives. provides a variety of resources for providers – as well as materials for their patients – to help encourage universal prenatal testing for HIV.

Mission Statement:

The mission of the *One Test. Two Lives.* campaign is to help prevent transmission of HIV from mother to child and promote optimal maternal health.

NOW AVAILABLE:

FREE EDUCATIONAL MATERIALS FOR OFFICE AND PATIENTS

CDC Resource Kit: HIV Screening of Pregnant Women (information sheets, pamphlets, posters): download or order free materials.

CONTACT:

CDC National Prevention Information Network (NPIN) at 800-458-5231 or E-mail: info@cdcnpin.org

CDC Prenatal HIV Testing Information

www.cdc.gov/1test2lives

CDC RECOMMENDATIONS

The New Jersey law closely follows the CDC's Revised Recommendation for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings (2006). The CDC urges that testing be done "as early as possible" in pregnancy and again, in some situations, in the third trimester. Early testing provides the opportunity to intervene with antiretroviral therapy for the woman's health, if appropriate, and to prevent perinatal transmission. Legally, as well as ethically, the testing must be voluntary and free of coercion, and a woman may not be denied care if she declines HIV testing. The CDC also recommends that, if a woman declines a prenatal HIV test, the clinician should inquire as to the reason and offer the test again at a subsequent visit.²

THIRD TRIMESTER TESTING

Another key component of the New Jersey law is repeat HIV testing in the third trimester of pregnancy. **The CDC recommends a second HIV test in the third trimester in geographic areas like New Jersey with elevated HIV incidence (>17 cases per 100,000 person-years).** Surveillance has shown that an increasing proportion of women whose HIV was undiagnosed at delivery had seroconverted during pregnancy, increasing the risk of HIV transmission to the infant.² The New Jersey legislation follows CDC's recommendation for third trimester testing. While repeat HIV testing has been done for medical indications in New Jersey, routine third trimester testing will be a new and challenging requirement for OB providers. Like HIV testing in early pregnancy, third trimester testing uses an opt-out approach, including HIV with other tests, unless the woman declines.

The legislation and the CDC are silent about the specific timing of third trimester testing. The NJDHSS may make recommendations in its regulations or "best practices" documents, but OB clinicians will need to decide how best to integrate third trimester testing into routine care.

Should the test be done early in third trimester when other routine tests are done or should it be done closer to 34 weeks in order to lengthen the interval between the first and second HIV tests? Those issues will need to be resolved in the coming months.



The New Jersey Law follows the CDC's revised recommendation for HIV testing of adults, adolescents, and pregnant women in health-care settings (2006). The CDC urges that testing be done "as early as possible" in pregnancy and again, in the third trimester.



NEW JERSEY LEGISLATIVE MANDATE

The New Jersey law also follows the CDC recommendation that a rapid HIV test be offered to any woman presenting in labor without her HIV status documented in the medical record.

She should be provided with the same information given at the prenatal visits. The Standard of Care from the New Jersey Department of Health and Senior Services recommends a rapid HIV test.³ Rapid HIV testing in labor and delivery offers the possibility of providing antiretroviral prophylaxis to the pregnant woman during labor and to her newborn infant, if she is found to be HIV positive. Many New Jersey hospitals already offer rapid testing in labor and delivery for women whose HIV status is not documented. Those delivery hospitals which do not routinely offer paid HIV testing will need to put procedures in place for assessing the woman's HIV status, informing women that HIV is included in the tests ordered in the labor setting, including HIV testing in medical orders in the peripartum setting, and assuring that zidovudine is available in intravenous formulation for women in labor and as an oral syrup for newborns.

Some women may enter prenatal care or present in labor knowing that they have HIV infection, but may be reluctant to share that information with providers. Routine testing in the third trimester and in labor and

delivery afford other opportunities to encourage testing. **Clinicians must carefully follow up with any woman who declines testing to learn her reasons and to reassure her that HIV testing is not risk-based and is routine across New Jersey for pregnant women.**

Newborn rapid HIV testing is also required in some situations under the new legislation. If a mother's HIV status is still unknown or undocumented when the infant is born, the birthing facility is required to test the newborn.

The antibody testing of the newborn will reveal a mother's HIV status since the infant has maternal HIV antibody if the mother is infected. **Newborn testing should be done as soon as possible after birth since the USPHS recommendations for newborn prophylaxis recommend infant prophylaxis with oral zidovudine be initiated preferably within 6-12 hours of birth.**⁴ Birthing facilities which are not already monitoring maternal HIV status will need to assure that a mother's HIV status is documented in the record sent to the newborn nursery and that routine HIV testing is included as a standing admission

order for newborns whose mother's status is unknown. ARV prophylaxis with oral zidovudine syrup will need to be available for the infant in the hospital and at home for six weeks following discharge. Parents may refuse testing of their newborns for religious reasons if they object in writing.

Follow-Up For HIV-Exposed Newborns

The legislation also requires that NJDHSS establish a comprehensive follow-up testing program for HIV-exposed newborns who test HIV positive or whose mothers tested positive. Those services are already in place in most locales through the services of the New Jersey Family-Centered HIV Care Network. The network has seven sites across the state that receive funding from NJDHSS through a federal grant from Part D of the Ryan White CARE Act (www.nj.gov/health/fhs/hivcare/regional.shtml).

The pediatric HIV specialists and multi-disciplinary care teams at these programs have provided expert HIV care to children and families across New Jersey for nearly twenty years and are well-positioned to provide diagnostic testing and ongoing care for newly identified HIV-exposed infants and their families. HIV-exposed infants will require a schedule of HIV diagnostic testing and follow-up care. The diagnosis and management of HIV-infected infants is discussed in detail in another USPHS document, *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*, which is also a "living document" updated regularly by the Pediatric ARV Working Group at the AIDSInfo site (www.aidsinfo.nih.gov).



Perinatal HIV Prevention and the 2007 New Jersey Legislation

CARE OF PREGNANT HIV-POSITIVE WOMEN

The New Jersey legislation will pose some challenges for providers but it also affords the hope that every pregnant woman with HIV infection and every HIV-exposed infant will be identified early and linked into care for diagnosis and treatment. A woman whose HIV infection is identified early in pregnancy will have the opportunity for comprehensive management of her HIV infection, with the promise for optimizing her own health and for decreasing her infant's risk of HIV.

Use of Antiretroviral Agents

With active management of a pregnant woman's HIV infection with antiretroviral (ARV) therapy, cesarean section when appropriate, and avoidance of breast feeding, the risk of HIV transmission from mother-to-child can be as low as 1%. The US Public Health Service Panel's (the Panel) 2007 Recommendation for Antiretroviral (ARV) Drugs in Pregnant Women and to Reduce Perinatal HIV Transmission (the Perinatal Guidelines) discuss in detail the management of pregnant women with HIV infection. The Perinatal Guidelines are a "living document" available online through the U.S. government site, AIDS Info (www.aidsinfo.nih.gov) and are updated regularly by the Panel. For the most current recommendations, check the online version.

In the November 2007 Guidelines, the Panel reaffirmed the importance of providing a three-part regimen of ARV drugs during pregnancy, labor, and postpartum to the infant. The three part regimen for the use of zidovudine (AZT, ZDV) is shown in Table 1 below. They also reiterated the enhanced effectiveness of combination ARV treatment and prophylaxis rather than single drug treatment. The Panel reaffirmed its long-standing recommendation that ARV prophylaxis should be offered to all pregnant HIV-infected women regardless of CD4+ count or HIV RNA copy number. ⁴

In brief, the Perinatal Guidelines discuss ARV treatment and prophylaxis for pregnant women with HIV in several clinical situations outlined in Table 2.



Table 1. Pediatric AIDS Clinical Trials Group (PACTG) 076 Zidovudine (ZDV) Regimen⁴

Time of Zidovudine (ZDV) Administration	Regimen
Antepartum* *Current Guidelines recommend ZDV be used as a component of a 3 drug highly active antiretroviral therapy (HAART) regimen	Oral administration of 100 mg ZDV five times daily, initiated at 14 to 34 weeks gestation and continued throughout the pregnancy Note: Oral ZDV administered as 200 mg three times daily or 300 mg twice daily is currently used in general clinical practice and is an acceptable alternative regimen to 100 mg orally five times daily.
Intrapartum	During labor, intravenous administration of ZDV in a one-hour initial dose of 2 mg/kg body weight, followed by a continuous infusion of 1 mg/kg body weight/hour until delivery.
Postpartum	Oral administration of ZDV to the newborn (ZDV syrup at 2 mg/kg body weight/dose every 6 hours) for the first 6 weeks of life, beginning at 8 to 12 hours after birth. Note: Intravenous dosage for full-term infants who cannot tolerate oral intake is 1.5 mg/kg body weight intravenously every 6 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.

Table 2. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-1-Infected Women and Prevention of Perinatal HIV-1 Transmission in the United States⁴

Clinical Situation	Recommendation
HIV-1-infected woman of childbearing potential but not pregnant, & who has indications for initiating antiretroviral therapy	<ul style="list-style-type: none"> • Initiate HAART as per adult treatment guidelines. • Avoid drugs with teratogenic potential (EFV) in women of child-bearing age unless adequate contraception ensured. Exclude pregnancy before starting treatment with EFV.
HIV-1-infected woman who is receiving HAART and becomes pregnant	<p>Woman:</p> <ul style="list-style-type: none"> • Continue current HAART regimen if successfully suppressing viremia, except avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddl). • Pregnant women receiving nelfinavir should be switched to an alternative regimen until further notice unless no other alternative is available. • HIV antiretroviral drug resistance testing is recommended if the woman has detectable viremia on therapy. • In general, if woman requires treatment, antiretroviral drugs should not be stopped during the 1st trimester. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion* during labor while other antiretroviral agents are continued orally) and postpartum. • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV-1 RNA remains >1,000 copies/mL near the time of delivery. <p>Infant: ZDV for six weeks started within 6-12 hours after birth.†</p>
HIV-1-infected pregnant woman who is antiretroviral naïve and has indications for antiretroviral therapy	<p>Woman:</p> <ul style="list-style-type: none"> • HIV antiretroviral drug resistance testing is recommended prior to the initiation of therapy, and if suboptimal viral suppression after initiation of HAART. • Initiate HAART regimen. <ul style="list-style-type: none"> – Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddl). – Nelfinavir should not be used during pregnancy until further notice unless no other alternative is available. – Use of ZDV as a component of the antiretroviral regimen is recommended when feasible. – NVP can be used as a component of HAART for women with CD4⁺ cell count <250 cells/mm³, but should only be used as a component of therapy in women with CD4⁺ cell counts >250 cells/mm³ if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • For women who require immediate initiation of therapy for their own health, treatment should be initiated as soon as possible, including in the first trimester. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion¹ during labor while other antiretroviral agents are continued orally) and postpartum. • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV-1 RNA remains >1,000 copies/mL near the time of delivery. <p>Infant: ZDV for six weeks started within 6-12 hours after birth.†</p>
HIV-1-infected pregnant woman who is antiretroviral naïve and does not require treatment for her own health	<p>Woman:</p> <ul style="list-style-type: none"> • HIV antiretroviral drug resistance testing is recommended prior to the initiation of therapy, and if suboptimal viral suppression after initiation of HAART. • HAART is recommended for prophylaxis of perinatal transmission in women who do not require treatment for their own health. <ul style="list-style-type: none"> – Consider delaying HAART initiation until after first trimester is completed. – Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddl). – Nelfinavir should not be used during pregnancy until further notice unless no other alternative is available. – Use of ZDV as a component of the antiretroviral regimen is recommended when feasible. – NVP should only be used as a component of therapy in women with CD4⁺ cell counts >250 cells/mm³ if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Use of ZDV prophylaxis alone is controversial, but may be considered for those women with plasma HIV-1 RNA levels less than 1,000 copies/mL on no therapy.

(Continued)

Table 2. Clinical Scenario Summary Recommendations for Antiretroviral Drug Use by Pregnant HIV-1-Infected Women and Prevention of Perinatal HIV-1 Transmission in the United States⁴

Clinical Situation	Recommendation
	<ul style="list-style-type: none"> • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion* during labor while other antiretroviral agents are continued orally). • Evaluate need for continued therapy postpartum; discontinue HAART unless has indications for continued therapy (if regimen includes drug with long half-life like NNRTI, consider stopping NRTIs 7 days after stopping NNRTI although limited data). • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV-1 RNA remains >1,000 copies/mL near the time of delivery. <p>Infant: ZDV for six weeks started within 6-12 hours after birth.†</p>
HIV-1-infected pregnant woman who is antiretroviral experienced but not currently receiving antiretroviral drugs	<p>Woman:</p> <ul style="list-style-type: none"> • Obtain full antiretroviral treatment history and evaluate need for antiretroviral treatment for own health. • Perform HIV-1 antiretroviral drug resistance testing prior to initiating repeat antiretroviral prophylaxis or therapy, and if suboptimal viral suppression after initiation of HAART. • Initiate HAART, with regimen chosen based on resistance testing and prior therapy history. <ul style="list-style-type: none"> – Avoid use of EFV or other potentially teratogenic drugs in the first trimester and drugs with known adverse potential for mother (combination d4T/ddI). – Nelfinavir should not be used during pregnancy until further notice unless no other alternative is available. – Use of ZDV as a component of the antiretroviral regimen is recommended when feasible. – NVP should only be used as a component of therapy in women with CD4⁺ cell counts >250 cells/mm³ if the benefit clearly outweighs the risk due to an increased risk of severe hepatic toxicity. • Continue HAART regimen during intrapartum period (ZDV given as continuous infusion¹ during labor while other antiretroviral agents are continued orally). • Evaluate need for continued therapy postpartum; discontinue HAART unless she has indications for continued therapy (if regimen includes drug with long half-life like NNRTI, consider stopping NRTIs 7 days after stopping NNRTI although limited data). • Scheduled cesarean delivery at 38 weeks gestation if plasma HIV-1 RNA remains >1,000 copies/mL near the time of delivery. <p>Infant: ZDV for six weeks started within 6-12 hours after birth.†</p>
HIV-1 infected woman who has received no antiretroviral therapy prior to labor	<p>ZDV</p> <p>Woman: ZDV given as continuous infusion¹ during labor. • Infant: ZDV for six weeks started within 6-12 hours after birth.†</p> <p>OR</p> <p>Combination ZDV + Single-Dose NVP:</p> <p>Woman: ZDV given as continuous infusion¹ during labor, plus single-dose NVP[‡] at onset of labor. Consideration should be given to adding 3TC during labor and maternal ZDV/3TC for 7 days postpartum, which may reduce development of NVP resistance.</p> <p>Infant: Single-dose NVP[‡] plus ZDV for six weeks.</p> <p>OR</p> <p>Woman: ZDV given as continuous infusion[†] during labor.</p> <p>Infant: Some clinicians may choose to use ZDV in combination with additional drugs in the infant, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended.</p> <ul style="list-style-type: none"> • Evaluate need for initiation of maternal therapy postpartum.
Infant born to HIV-1-infected woman who has received no antiretroviral therapy prior to or during labor	<ul style="list-style-type: none"> • ZDV given for 6 weeks to the infant, started as soon as possible after birth. † <p>OR</p> <ul style="list-style-type: none"> • Some clinicians may choose to use ZDV in combination with additional drugs, but appropriate dosing for neonates is incompletely defined and the additional efficacy of this approach in reducing transmission is not known. Consultation with a pediatric HIV specialist is recommended. • Evaluate need for initiation of maternal therapy postpartum.

HAART: Highly active antiretroviral therapy, a minimum of three antiretroviral agents; ZDV: Zidovudine; 3TC: Lamivudine; NVP: Nevirapine; EFV: Efavirenz

* ZDV continuous infusion: 2 mg/kg ZDV intravenously over 1 hour, followed by continuous infusion of 1 mg/kg/hour until delivery.

† 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.

‡ Single dose NVP: Mother: 200 mg given once orally at onset of labor; Infant: 2 mg/kg body weight given once orally at 2-3 days of age if mother received intrapartum single dose NVP, or given at birth if mother did not receive intrapartum single-dose NVP.

The Guidelines recommend:

- That pregnant women who know their HIV status and are already taking ARV treatment continue on their treatment regimen if it is effectively suppressing viral load. However, efavirenz (EFV) should be avoided in the first trimester of pregnancy.
- If the woman has detectable viremia, she should undergo an adherence assessment and counseling in addition to ARV drug resistance testing. Consultation with an HIV expert is also recommended. The Guidelines provide detailed information on drug toxicity and pharmacokinetics in pregnancy.⁴



Although some obstetric providers have expertise in antiretroviral therapy, for most providers, it will be important to assure that established referral links are in place for women newly diagnosed with HIV during pregnancy.

Pregnant women with HIV who meet the standard criteria for initiation of ARV therapy in adults should receive a potent combination ARV therapy, usually three drugs, keeping in mind what is known about each drug in pregnancy. Women whose HIV infection has not progressed to the point where they meet the adult criteria should also receive a potent three-drug combination of ARVs for prophylaxis of perinatal transmission. For these women, delaying the start of ARVs until after the first trimester can be considered. Another increasingly common situation for women with HIV infection is those women who have previously been on ARV treatment or prophylaxis, but are not currently on ARVs. For these women, the Guidelines recommend initiating a potent three-drug treatment based on the results of her treatment history and resistance testing. The Guidelines continue to recommend avoiding drugs that are teratogenic e.g., EFV or have adverse effects in pregnant women. The Guidelines recommend HIV resistance testing for all HIV-infected pregnant women prior to the initiation of ARV therapy or prophylaxis and for women who continue to have a detectable viral load (HIV RNA).⁴



Women with HIV infection who have received no ARV therapy or prophylaxis during pregnancy, or who are newly diagnosed in labor, should have intrapartum IV zidovudine started immediately; and their infants should receive the six week course of oral zidovudine beginning a few hours after birth. The Panel recommends starting IV ZDV even before the results of a confirmatory HIV test are available. This intervention reduces the infant's risk of HIV transmission from 27% to 10%.⁵ A current clinical trial is assessing whether the addition of other drugs further reduces the risk of transmission. Some experts would expand the treatment of untreated women presenting in labor to include a single dose of nevirapine for mother at the onset of labor and for the infant at 48-72 hours. If nevirapine is added, the clinician should consider also administering lamivudine (3TC) to the mother and infant in order to decrease the risk of the mother developing resistance to nevirapine, which has a very long half-life.⁴ An additional discussion of the clinical judgment and research supporting the use of these additional ARV drugs can be found in the Guidelines.

The Guidelines continue to recommend avoiding drugs that are teratogenic, e.g., EFV, or have adverse effects in pregnant women.

Labor and Delivery

In New Jersey, women who present in labor with unknown HIV status represent the major missed opportunity to the maximal reduction of vertical HIV transmission. The key to reducing the risk of HIV transmission for these women is to conduct rapid HIV testing and start ARV prophylaxis with IV ZDV as soon as possible if found positive. The CDC-sponsored Mother-Infant Rapid Intervention at Delivery (MIRIAD) study showed that offering voluntary HIV testing during labor is feasible in obstetrical settings.

In addition, point-of-care rapid HIV testing has been shown to provide results faster than sending specimens to the hospital laboratory for rapid HIV testing.⁷ Rapid HIV testing is recommended for women in labor whose HIV status is unknown or undocumented.⁸ The NJDHSS has established a standard of care in which women who present in labor with unknown HIV status should receive counseling, be offered voluntary rapid HIV testing, and, if a preliminary rapid HIV test result is positive, be offered ZDV for the mother as well as the infant with referral to a physician with experience and expertise treating HIV disease.³

A significant number of newborns become infected during labor and delivery. Although the exact mechanism of transmission is unknown, it may occur through transplacental microtransfusion of blood during uterine contractions or by exposure to the virus in the cervicovaginal secretions during delivery.

A cesarean delivery prior to the onset of labor and before the rupture of membranes reduces the risk of vertical HIV transmission for women whose viral load exceeds 1,000 copies per milliliter. The American College of Obstetrics and Gynecology and The *USPHS Panel* recommend a scheduled, elective caesarian section at 38 weeks of completed gestation for women whose viral load exceeds 1,000 copies per milliliter. Viral load monitoring is recommended every three months in pregnancy or following changes in ARV therapy. The most recent viral load results should be used to determine the mode of delivery. For women whose viral load is less than 1,000 copies per milliliter, the risk of cesarean delivery outweighs the potential benefits.^{4,6} Clinicians should individualize their assessment of the risks and benefits of cesarean section for a woman and her infant if she has gone into labor or her membranes have ruptured.⁴

A SIGNIFICANT NUMBER OF NEWBORNS become infected during labor and delivery. Although the exact mechanism of transmission is unknown, it may occur through transplacental microtransfusion of blood during uterine contractions or by exposure to the virus in the cervicovaginal secretions during delivery. A cesarean delivery prior to the onset of labor and before the rupture of membranes reduces the risk of vertical HIV transmission for women whose viral load exceeds 1,000 copies per milliliter.



Perinatal transmission rates can be 2% or less if HIV is detected and treated early.



Health Care Provider Resources:

The website for the *One Test. Two Lives.* campaign from the Centers for Disease Control and Prevention (CDC) includes links to key documents relevant to HIV testing in pregnancy for download:

- MMWR: Revised Recommendations for HIV Screening of Pregnant Women
- Fact Sheet: Routine Prenatal Testing: The Opt-Out Approach Q&A
- Guidance Document: Rapid HIV Antibody Testing During Labor and Delivery for Women of Unknown HIV Status: A Practical Guide and Model Protocol

Committee opinions/statements available for download include:

- Recommendation Statement: Screening for HIV from the U.S. Preventive Services Task Force
- ACNM Position Statement on Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS)

CONTACT:

CDC National Prevention Information Network (NPIN)
800) 458-5231 or
E-mail: info@cdcnpin.org
www.cdc.gov/1test2lives

Prenatal HIV Testing Information
One Test. Two Lives.

Care of the Newborn

A pediatric HIV specialist should be consulted to follow all HIV exposed newborns. ARV prophylaxis for the newborn should be discussed and correct administration taught to the mother. All HIV-exposed newborns should receive ZDV syrup 2mg/kg orally every six hours for six weeks beginning at 6-12 hours after birth. Additional ARV medications for infants born to mothers with no or minimal ARV use or suboptimal viral suppression may be recommended. A complete blood count (CBC) and differential should be performed on the newborn at baseline before administration of ZDV.⁴

Because the results of an HIV antibody testing for a newborn will reflect the mother's HIV antibody status, follow-up testing using viral tests is recommended. The preferred virologic assays are HIV DNA PCR or HIV RNA. The Pediatric Guidelines now recommend viral testing at 14-21 days of age, 1-2 months of age, and 4-6 months of age. Some HIV experts will conduct viral testing at birth as well. According to the USPHS, HIV infection is diagnosed by two positive HIV viral tests performed on separate blood samples, regardless of age.

HIV infection can be presumptively excluded in non-breastfed infants with:

- Two or more negative viral tests (one at >14 days of age and one at >1 month of age)
- One negative viral test at >2 months of age
- One negative HIV antibody test at >6 months of age⁴

Prophylaxis against PCP pneumonia with TMP-SMX should be started at 4-6 weeks of age for all HIV-exposed infants until it is determined that the child is uninfected or presumptively uninfected.⁴ Additional guidance on follow-up of HIV-exposed and infected children can be found in the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection, February 2008.



Summary

Proper prenatal and newborn care can reduce the risk of vertical HIV transmission.

The New Jersey legislation on HIV testing of pregnant women and newborns holds the promise of earlier identification of pregnant women living with HIV infection who may not know their HIV status. ♦ Women who previously may not have been offered or might not have accepted HIV testing will have the HIV test included with other prenatal tests unless they opt out. ♦ Third trimester testing will identify women who seroconvert during pregnancy. ♦ Women presenting very late in care or in labor will be offered rapid HIV testing. ♦ Each of these testing opportunities has the power to identify pregnant women with HIV and engage them in interventions to decrease the risk of HIV transmission to their infants. ♦ The different ARV treatment and prophylaxis options available are detailed in the Perinatal Guidelines. ♦ The final safety net of newborn testing will hopefully identify only a handful of HIV-exposed infants, but still offers an opportunity to reduce perinatal transmission risk. ♦ When implemented state-wide, the strategies in the law should move New Jersey closer to a time when perinatal HIV transmission is eliminated and women with HIV infection are identified early in the course of their disease.

New Jersey Provider Guide to Rapid HIV Testing in Labor & Delivery

Providing Information to Women in Labor with Unknown HIV Status Regarding Routine, Rapid HIV-1 Antibody Testing

Eligibility: P.L. 2007.c.218 requires that all pregnant women routinely have an HIV test early in prenatal care, a repeat test in the third trimester, and if the pregnant woman's HIV status is unknown, a rapid test in labor and delivery. A woman may decline testing; however, her newborn will be tested if the mother's HIV status is unknown unless the woman refuses infant testing on religious grounds.

Script: A guide to help you inform women in labor about routine rapid HIV testing and its importance in preventing perinatal HIV transmission, as required by law. Background information/instructions are in red bold type; words you can use are in black type.

- It is important to show empathy while you are talking with the laboring woman, through your body language and/or through holding her hand/ touch.
- Tell the woman she should signal you when a contraction is happening, so you can pause until it is over.
- Pause to verify understanding. Adjust your terminology as needed.
- Tell the woman that the discussion about HIV testing will be kept confidential

Before discussing HIV testing, ensure that the woman is between contractions, that she is fairly comfortable, and that she is alone (no family member or significant other is present in the room, or within hearing). Tell her that you are going to talk to her about HIV testing, and ask if she wants her partner or family member to be present.



Introduction to HIV testing in labor & delivery:

- HIV rapid testing is routine in New Jersey for all women in labor who have not had an HIV test in the third trimester.
- We don't have any record of your HIV test results in the last three months.
- We routinely do a rapid HIV test during labor because so much can be done to protect the baby if the mom has HIV. We also do it to help women live a healthier, longer life.

I have three things I am going to talk to you about:

- A special HIV/AIDS test that is required by law in New Jersey
- Why this test is important for you and your baby, AND
- What happens when the test result comes back

A special HIV/AIDS test is required by law in New Jersey

- It is important for you and your baby that you have a "rapid" HIV test. HIV is the virus that causes AIDS.
- This test can give us results quickly.
- If you decline to have the test, the law requires that we test your baby after birth.

Why this test is important

- Human Immunodeficiency Virus (HIV) is the virus that causes AIDS.
- HIV is a serious illness that can affect a woman's health and her baby's health.
- One of the ways HIV is spread is by unprotected sex. Therefore, all pregnant women may be at risk for HIV infection.
- HIV can be passed from a mother to her baby during pregnancy, at delivery, and through breastfeeding.
- If you have HIV infection, rapid testing will allow you to get medication during labor and delivery, to reduce the risk of passing HIV to your baby.
- Your baby will receive the same medication after birth.
- Without treatment, the chance the baby will be infected is about 25%, or 1 in 4 babies.
- We know if women are given medication during labor and delivery and their babies get the medication right after birth, we can reduce the risk of HIV transmission to about 10%, or 1 in 10 babies.

What happens when the test result comes back:

- You will receive a preliminary result about an hour after your blood is drawn.
- If the rapid HIV test is negative, no further testing is needed at this time. It is most likely that you do not have HIV. However, the test may not show very recent infection.
- If the rapid test is negative, it is OK to breast feed your baby.

If the rapid HIV test is positive:

You probably have HIV infection and your baby may have been exposed to HIV.

- The test is a screening test that provides a preliminary result, and a false-positive result can happen.
- We always do a second test to confirm rapid tests that are positive.
- To be safe, it is best to start medicines to help prevent transmission of HIV to your baby, while we wait for the confirmatory test result.
- Experts recommend several medicines to reduce the chance your baby will get HIV. One is called AZT and it is given through your IV fluids into your vein. The other is a pill called nevirapine.

Medical Treatment:

Your doctor will decide which medicines will be best for you and your baby and will discuss them with you before starting them. After your baby is born, he/she will start taking AZT syrup.

- These medicines have been studied in pregnant women and newborns and there have been no serious side effects.
- You should wait until we have the results of the confirmatory test before you start breastfeeding.

If the confirmatory test is negative:

- You and your baby will immediately be taken off any medication that was started.

If the test is confirmed as positive:

- All medication that was started to help prevent HIV transmission will continue
- If treatment is started, a doctor or nurse will discuss again any consequences of taking the medication.
- Your baby will need more testing for HIV infection.

You will be referred to a physician for your own medical care – there are also medications to help keep you healthy longer. You will also be referred to a health care provider who will take care of your baby's medical needs.

- HIV test results are confidential. There are laws to protect people with HIV from discrimination.

CASE

Preconception Counseling of HIV+ Women

TC is a 38-year-old woman, treated for HIV for 12 years, now a biomedical engineer. Her HIV was stable and monitored for many years without ARV treatment, and she continued to come to Newark to see the infectious disease physician about twice a year even after she moved to Texas for her job several years ago. She has support from her family, but few others know of her HIV status. She had a long-term relationship with her HIV-negative male partner.

About 2 years ago, TC's CD4⁺ count dropped to the low 300s, though her VL was only 60,000. She discussed treatment options and decided with the physician to begin ARV therapy. Her initial regimen was Combivir + Sustiva, which she tolerated well, although her first night had the unsettling side effect of hallucinations that left her very shaky at work the next day. She has been 100% adherent and very motivated to stay healthy. About a year ago, TC came in to discuss how she and her partner could have a child, and wanted to actively plan a healthy outcome.

**Overall goals**

- Stabilize HIV: undetectable viral load, high CD4⁺
- Taking and adherent to antiretroviral treatment
- Preventing transmission to partner
- Close monitoring of viral load, health (note: CD4⁺ counts often decrease in pregnancy)

Concerns addressed by the physician

Antiretroviral concerns: the physician wants to get her off Sustiva before pregnancy, to reduce the risk of teratogenic effects; her preferred regimen would include protease inhibitors for reducing perinatal HIV transmission. Drawback of protease inhibitors: this patient was at high risk of potential side effects. Viramune has been found to have side effects of liver toxicity and hepatic necrosis in women who are overweight or have a higher CD4⁺ count. TC had a history of non-insulin dependent diabetes, which she had gotten under control via diet and exercise, and maintained a slightly high weight though she was not obese, and she also had a relatively high CD4⁺ count.

Reducing the chance of transmission to the HIV-negative partner

The couple agreed to continue their existing practice of using contraception including condoms, and to minimize transmission risks by choosing one of several options:

- Self-insemination, or
- Unprotected intercourse just during her fertile time, as determined by basal thermometer, or Physician-assisted insemination

Implementing the plan

The physician and TC opted to switch from Sustiva to Kaletra, and continued the Combivir. Her LFTs and all other labs were normal, and her CD4⁺ count has been in the 700-900 range, with an undetectable VL. TC's preference was to have physician-assisted insemination.

Roadblock to the plan to get pregnant

TC and her boyfriend broke up. She still wants to have a baby and feels she is running out of time, at age 38. She is staying on Kaletra and may try to become pregnant through donor insemination, which would place no risk to her or a partner. So far she has found that her options include the assisted fertility programs at UMDNJ and Columbia University, or she could travel to Italy for IVF.

CASES FROM THE PERINATAL HIV HOTLINE

Provided by Shannon Weber, MSW, Perinatal HIV Hotline Coordinator for the National HIV/AIDS Clinicians' Consultation Center with commentary from Patricia Kloser, MD, MPH, UMDNJ-University Hospital, Newark.

Case 1. A Hotline Call

A 37-year-old woman at 39 weeks gestation presents to Labor and Delivery with frequent contractions and at 5cm dilatation. A rapid HIV test is weakly positive. The patient had refused HIV testing during prenatal care. She denies any risk factors, but her husband is known to be HCV-positive.

- Should HIV medications be initiated?
- What tests or treatment should be prescribed for the infant?
- What follow up testing is need to confirm the womans HIV status?

Women with a positive rapid HIV test should be presumed to be infected until a confirmatory Western blot can clarify their status.

Intravenous zidovudine should be started immediately to reduce the chance of perinatal HIV transmission and should be continued until the cord has been clamped. The infant should be started on oral zidovudine as close to birth as possible (within 6-12 hours).

Consideration can also be given to adding a single dose of nevirapine to the mother before delivery and to the infant at 48-72 hours of life, although there are no data to assess whether this will further decrease the chance of transmission. If the mother receives nevirapine, she should be given oral zidovudine and lamivudine for one week to reduce the chance of developing nevirapine resistance.

If the mother's Western blot is negative, she is not HIV-infected and has a false positive HIV ELISA test. All antiretrovirals can be discontinued in the mother and infant.



Case 2. Prenatal Testing Issues: Why is Rapid Testing Needed?

Presentation posted: Pacific AETC webpage: <http://www.sfaetc.ucsf.edu/RTL/RTLManual/slides/9-20CCPrenatalTestingIssues.htm>
 Provided by Cynthia Carmichael, MD, Deputy Director, Contra Costa County and Faculty, East Bay AETC, North Richmond Center for Health

2006 Case #1: "I just got tested"

- Mom and dad want to have a baby.
- Both get tested and are HIV Ab negative.
- 3-4 months later they conceive a baby.
- Mother was offered testing at a prenatal visit but declined because "I just got tested" and "neither of us has outside relations".
- Baby born, full term, stable, AGA.
- Thrush in first 2 months.
- Admitted at 3 months with respiratory distress, failure to thrive, severe thrush, axillary adenopathy... then confirmed to have HIV, PCP, and CMV.
- Labs: CD4⁺ 342, HIV RNA PCR >750,000.
- Currently on ZDV, 3TC, Kaletra, EPO, Fe, GCSF, Ganciclovir, TMP-SMX, azithromycin, fluconazole, and amlodipine through a Broviac.
- Also requires NG feeds, hyperal through a Broviac.

This case was revisited to determine how HIV was missed in prenatal care and early pediatric care.

PRENATAL CARE:

- Mother was offered testing at a prenatal visit but declined because "I just got tested" and her complete statement was: "Neither of us has had outside relations since we've been together."

NEWBORN CARE:

- Baby breastfed x 1 month
- Intermittent breastfeeding
- Admitted at 3 months with big liver... then confirmed to have PCP, CMV and HIV.

Dr. Kloser comments: This is an example of the need to obtain "source" documentation for HIV tests done outside the clinician's practice, and to repeat the HIV test in all women in the third trimester. New HIV infections are particularly dangerous for the fetus because of the very high viral load before antibodies develop. It is imperative to begin HAART and have rapid decrease of viral load to prevent in utero or peripartum acquisition of HIV. Many babies have thrush, but respiratory distress is especially concerning.

Perinatal HIV Prevention and the 2007 New Jersey Legislation

REFERENCES

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- New Jersey Department of Health and Senior Services. Standard of Care for Women who Present in Labor with Unknown HIV Status. www.state.nj.us/health/aids/stdcare.pdf
- Public Health Service Task Force. (2007) Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the U.S. Available <http://AIDSinfo.nih.gov>. Accessed May 4, 2008.
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SAVE THE DATE

October 14, 2008

Reducing Mother-to-Child HIV Transmission in New Jersey

New Jersey Hospital Association • Conference Center • Princeton, NJ



*This conference is sponsored by
UMDNJ and the New Jersey Department of Health and Senior Services,
Division of HIV/AIDS Services.*



Poster Topics and Abstract Submissions:

This Call for Posters invites health care providers to submit abstracts detailing on-going research projects and/or innovative strategies in the area of reducing perinatal transmission of HIV.

Abstracts should address at least one of the following key areas that impact perinatal transmission: Obstetrical Care, Counseling and Testing, HIV-exposed Infant Care, Epidemiology/Surveillance, Healthcare Policy and Access/Retention in OB/GYN Care.

Deadline for submission is August 22, 2008.

For questions about poster abstract submission, please contact Michelle Thompson at ccthompson@umdnj.edu or by phone at 973-972-1293 or 973-972-3690.

FOR MORE INFORMATION AND TO REGISTER:

<http://ccoe.umdnj.edu/catalog/aids> or call 973-972-3690

UMDNJ-Center for Continuing & Outreach Education-Division of AIDS Education

RESOURCES FOR FURTHER INFORMATION AND CARE IN NEW JERSEY

Healthy Start

■ Camden Healthy Start Project

2600 Mt. Ephraim Ave., Camden, NJ 08104 • (856) 963-1013

■ Isaiah House-Healthy Start Mother & Child Program

422 Main St., East Orange, NJ 07018 • (973)-678-5882

■ Trenton Healthy Start Project

16 East Hanover St., Trenton, NJ 08618 • (609) 989-3307

New Jersey Maternal Child Health Consortia

■ Southern NJ Perinatal Cooperative, Inc.

2500 McClellan Avenue, SUITE 250, Pennsauken, NJ 08109
(856) 665-6000 • FAX (856) 665-7711 • www.snjpc.org

■ Hudson Perinatal Consortium, Inc.

242 10th Street, Jersey City, NJ 07302
(201) 876-8900 • FAX (201) 876-2670 • www.hudsonperinatal.org

■ Central NJ MCH Consortium

2 King Arthur Court, Suite B, North Brunswick, NJ 08902
(732) 937-5437 • FAX (732) 937-5540 • www.cnjmchc.org

■ Gateway Northwest Maternal and Child Health Network

381 Woodside Avenue, Newark, NJ 07104
(973) 268-2280 • FAX (973) 268-2283 • www.gatewaymch.org

■ Regional Perinatal Consortium of Monmouth & Ocean Counties, Inc.

725 Airport Road, Suite 1C, Lakewood, NJ 08701-5900
(732) 363-5400 • FAX (732) 363-5554 • www.rpcmoc.org

■ Northern NJ MCH Consortium

17 Arcadian Avenue, Suite 204, Paramus, NJ 07652
(201) 843-7400 • FAX (201) 843-4988 • www.maternalchildhealth.org

Resources for Further Information

■ National Perinatal HIV Consultation and Referral Service

<http://www.nccc.ucsf.edu/Hotlines/Perinatal.html>

Perinatal HIV Hotline

(888) 448-8765 or [(888) HIV-8765]

Free 24-hour clinical consultation and advice on:

- Management of HIV in pregnant women
- HIV testing in pregnancy
- Care of HIV-exposed infants

Perinatal HIV Network

- Links callers with local perinatal HIV specialists

HIV Rapid Testing in Labor and Delivery (RTLDD) Resources & Reference Manual

<http://www.sfaetc.ucsf.edu/RTLDD/index.html>

• CDC practical guide and model protocol

http://www.cdc.gov/hiv/rapid_testing/rt-labor&delivery.htm

National Perinatal HIV Treatment Guidelines

www.aidsinfo.nih.gov

■ American College of Obstetricians and Gynecologists

<http://www.acog.org> • (202) 638-5577

■ American College of Nurse-Midwives

<http://www.acnm.org> • (240) 485-1800

■ Women, Children, and HIV

www.womenchildrenhiv.org

Links re: HIV counseling & testing and perinatal interventions for women, infants, and children. Resources include clinical guidelines and tools, training and community education materials, journal scan, and conference abstracts.

Resource Centers in the Ryan White Part D New Jersey Statewide Family Centered HIV Care Network

University of Medicine & Dentistry of New Jersey (UMDNJ)

Francois Xavier Bagnoud Center
65 Bergen St., Rm 823, Newark, NJ 07103
(973) 972-0400

Newark Beth Israel Medical Center

Infectious Disease/Pediatrics
Family Treatment Center, G3
201 Lyons Ave., Newark, NJ 07112
(973) 926-8004

St. Joseph's Hospital & Medical Center

703 Main St., Paterson, NJ 07503
(973) 754-4713

Jersey City Medical Center

Center for Comprehensive Family Care
935 961 Garfield Ave., Jersey City, NJ 07304
(201) 915-2294

UMDNJ-Robert Wood Johnson Medical School

Department of Pediatrics
Division of Allergy,
Immunology & Infectious Diseases
Allergy, Immunology & Infectious Diseases
1 Robert Wood Johnson Place
PO Box 19, New Brunswick, NJ 08903
(732) 235-7894

Jersey Shore University Medical Center

Pediatric Sub-Specialty
1944 Corlies Avenue, Medical Arts Building
Suite 204, Neptune, NJ 07754
(732) 776-4271

Cooper Hospital/University Medical Center

Department of Pediatrics
3 Cooper Plz., Suite. 200, Rm. 202
Camden, NJ 08103
(856) 342-2617



Questions refer to the content of the article and the notes that follow. To receive CME/CE/CEU credit: complete exam, registration, and evaluation forms on-line at www.umdny.edu/ccoe/aids or fill in the forms on the following pages, and mail or fax to UMDNJ-CCOE (see Registration Form).

Questions 1 through 4 are based on the following case: Case: HIV+, pregnant woman seen in ID Clinic

DN is a 27-year-old woman who has been intermittently in care, using street meth and pills, and just out of jail. After an absence of almost a year, she came in this week, 18 weeks pregnant. She says she has just decided to go through with the pregnancy and asked if she can return to taking her previous combination ARVs. The physician's assessment is that DN's drug use and homelessness are the greatest risks to her ability to have a healthy pregnancy and healthy baby.

1. What is the physician's primary message to DN in this first visit since she has decided to continue her pregnancy?

- A. The physician will continue to be her HIV medical provider throughout her pregnancy and beyond.
- B. She will need to transfer to a prenatal/OB service.
- C. She will have an excellent chance of having a healthy, HIV-negative baby if she takes antiretroviral medication and gets prenatal care.
- D. She will need to stop using drugs and get housing if she wants to keep her baby.

2. What is your immediate goal for this first visit with DN since she has decided to continue her pregnancy?

- A. Re-engaging the patient in care.
- B. Transferring patient to prenatal/OB service
- C. Making sure the patient understands the HIV antiretroviral protocol she will receive to reduce transmission and support a healthy pregnancy.
- D. Ordering laboratory tests to determine HIV resistance profile, CD4+ count, viral load, and pregnancy staging.

3. What should an OB/Gyn practitioner, who is not also an HIV specialist, do in conjunction with the infectious disease practitioner?

- A. Refer this patient to ID practitioner for prenatal care and delivery.
- B. Provide both prenatal and HIV treatment, for the duration of the pregnancy.
- C. Develop labor and delivery plan including C-section.
- D. Develop labor and delivery plan including assessment of patient's HIV status close to delivery date, to determine if C-section is appropriate.

4. Which of the following interventions by the physician might interfere with the goals of a healthy pregnancy and reducing HIV transmission from mother to baby?

- A. The physician obtains a free lunch for the patient.
- B. The physician provides a renewal of the previous year's ARV prescriptions.
- C. The clinic nutritionist provides nutritional supplements for the next month, to encourage patient involvement in care.
- D. The infectious disease clinic provides prenatal vitamins as a first step toward prenatal care.

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5. **All of the following antiretroviral medications should be avoided in pregnancy. Which one has been identified as teratogenic?**
 - A. Nevirapine
 - B. Efavirenz
 - C. ddI/ Zerit
 - D. Kaletra in liquid formulation
6. **What antiretroviral should usually be part of the regimen for pregnant HIV patients?**
 - A. Nevirapine
 - B. Efavirenz
 - C. Zidovudine
 - D. Maraviroc
7. **Newborn HIV testing is required by the 2007 New Jersey legislation if:**
 - A. The mother did not have prenatal care.
 - B. The mother had unprotected sexual intercourse.
 - C. The mother's HIV status is not documented when the infant is born.
 - D. The mother has been receiving care in a drug treatment facility.
8. **An opt-out- approach to prenatal HIV testing includes each of the following EXCEPT:**
 - A. Information about the HIV test and why it is recommended.
 - B. Pre-test counseling and written informed consent.
 - C. Inclusion of HIV testing with other routine prenatal blood tests.
 - D. Continuing to provide medical care if the mother declines testing.
9. **The USPHS Perinatal Guidelines recommendations for HIV-infected pregnant women include all of the following except:**
 - A. The three part zidovudine prophylaxis regimen for all HIV-infected pregnant women.
 - B. HIV resistance testing before selecting HIV therapy.
 - C. Use of a combination for ARV drugs for therapy.
 - D. A scheduled cesarean section for all HIV-infected pregnant women.
10. **The 2007 New Jersey legislation on HIV testing of pregnant women and newborns requires:**
 - A. Opt-out HIV testing of pregnant women in the first and third trimesters as part of routine prenatal care.
 - B. Separate written informed consent for HIV testing of pregnant women.
 - C. Pre-test counseling for any HIV test.
 - D. Separate written informed consent for newborn HIV testing.



**CONTINUING
EDUCATION**

Perinatal HIV Prevention and the 2007 New Jersey Legislation

Registration Form

In order to obtain continuing education credit, participants are required to:

- (1) Read the learning objectives, and review the activity, and complete the post-test.
- (2) Complete this registration form and the activity evaluation form on the next page, and record your test answers below.
- (3) Send the registration and evaluation forms to: UMDNJ-Center for Continuing and Outreach Education
• VIA MAIL: PO Box 1709, Newark, NJ 07101-1709 • VIA FAX: (973) 972-7128
- (4) Retain a copy of your test answers. Your answer sheet will be graded and if you achieve a passing score of 70% or more, a credit letter awarding 1.25 AMA PRA Category 1 Credit(s)TM or 1.25 contact hours or 0.125 continuing education units, and the test answer key will be mailed to you within four (4) weeks.



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Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again.

Online option: This activity will be posted at www.umdj.edu/ccoe/aids where you will be able to submit your registration, quiz, and evaluation, and print your own credit letter.

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

POST-TEST <i>Circle the best answer for each question.</i>	1. A B C D	3. A B C D	5. A B C D	7. A B C D	9. A B C D
	2. A B C D	4. A B C D	6. A B C D	8. A B C D	10. A B C D

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- General:** Continuing Education Units (up to 1.25): Credits Claimed: _____

One credit for each hour of participation (ANCC, AMA); not to exceed 1.25 credits. Continuing Education Units: one unit per ten hours of participation.

I attest that I have completed the activity as designed. I will report the number of credits claimed above during my filing of continuing education credit with professional organizations, licensing boards or other agencies.

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**CONTINUING
EDUCATION**

Perinatal HIV Prevention and the 2007 New Jersey Legislation

Activity Evaluation Form

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants.



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Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:	Strongly Agree		Strongly Disagree		
<i>Objective 1:</i> Distinguish between routine and opt-out HIV testing protocols.	5	4	3	2	1
<i>Objective 2:</i> Outline the required information to provide to pregnant women before administering HIV tests under the 2007 New Jersey legislation.	5	4	3	2	1
<i>Objective 3:</i> Explain the increased emphasis on HIV testing in the third-trimester or at labor and delivery.	5	4	3	2	1
<i>Objective 4:</i> Summarize the interventions with HIV-positive women which can reduce perinatal transmission, from pre-conceptual counseling through post-delivery.	5	4	3	2	1

OVERALL EVALUATION:	Strongly Agree		Strongly Disagree		
The information presented increased my awareness/understanding of the subject.	5	4	3	2	1
The information presented will influence how I practice.	5	4	3	2	1
The information presented will help me improve patient care.	5	4	3	2	1
The faculty demonstrated current knowledge of the subject.	5	4	3	2	1
The program was educationally sound and scientifically balanced.	5	4	3	2	1
The program avoided commercial bias or influence.	5	4	3	2	1
Overall, the program met my expectations.	5	4	3	2	1
I would recommend this program to my colleagues.	5	4	3	2	1

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

Please provide any additional comments pertaining to this activity (positives and negatives) and suggestions for improvement. Please list any topics that you would like to be addressed in future educational activities:



Sponsorship

Sponsored by the University of Medicine & Dentistry of New Jersey (UMDNJ), UMDNJ-Center for Continuing & Outreach Education. This activity is supported by an educational grant from NJDHSS Division of HIV/AIDS Services through a MOA titled "Education and Training for Physicians and other Healthcare Professionals in the Diagnosis and Treatment of HIV/AIDS."

Target Audience

This activity is designed for physicians and nurses, and for other health care professionals in New Jersey who are involved in the care of persons with HIV/AIDS.

Statement of Need

The medical management of HIV has been revolutionized by the use of highly active antiretroviral therapy (HAART). In the pre-HAART era, HIV typically led to death within ten years. Treatment of HIV with HAART can extend the lifespan of HIV-infected persons several decades. A major challenge that has arisen out of this success is the management of the side effects of antiretroviral therapy. Antiretroviral therapy (ART) commonly causes various complications, some of which may be life threatening.

Abnormalities such as dyslipidemia, insulin resistance states, and lipodystrophy syndromes have become common metabolic complications associated with the treatment of HIV-infected persons, and may eventually lead to an epidemic of cardiovascular disease and diabetes among HIV-infected patients. Management of these complications has therefore become an integral component of HIV care.

Learning Objectives

Upon the completion of this activity, participants should be able to:

1. Describe metabolic complications associated with the use of antiretroviral agents.
2. Identify the risks and appropriate management of dyslipidemia for patients on antiretroviral agents.
3. Summarize the treatment of glucose intolerance in patients on antiretroviral agents.
4. Describe lipodystrophy and its management in patients on antiretroviral agents.

Method of Instruction

Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the post-test which consists of a series of multiple-choice and True/False questions.

Upon completing this activity as designed and achieving a passing score of 70% or more on the post-test, participants will receive a credit letter and the test answer key four (4) weeks after receipt of the post-test, registration, and evaluation materials. Estimated time to complete this activity as designed is 1.25 hours.

Accreditation

Physicians: UMDNJ-Center for Continuing & Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UMDNJ-Center for Continuing & Outreach Education designates this educational activity for a maximum of *1.25 Category 1 AMA PRA Credit(s)*[™]. Physicians should claim only credit commensurate with the extent of their participation in the activity.

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This activity is awarded 1.25 contact hours (60 minute CH).

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Review: This activity was peer reviewed for relevance, accuracy of content, and balance of presentation by Patricia Kloser, MD, MPH; and Brenda Christian, MEd, PA-C; and pilot tested for relevance and time required for participation by Kinshasa Morton, MD; Bonnie Abedini, RN, MSN; Linda Berezny, RN, BA; and Mary C. Krug, RN, MSN, APN-C.

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Faculty Disclosure Declarations

The following have no financial relationships to disclose: faculty: Mark J. Fussa, DO and Sindy M. Paul, MD, MPH, FACP; and reviewers: Patricia Kloser, MD, MPH; Brenda Christian, MEd, PA-C; Kinshasa Morton, MD; Bonnie Abedini, BSN, MS; Linda Berezny, RN, BA; and Mary C. Krug, RN, MSN, APN-C; and *New Jersey AIDSLine* editor Kimi Nakata, MSW, MPH.

Off-Label Usage Disclosure

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Disclaimer

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Metabolic Complications Associated with the Treatment of HIV-Infected Persons

Mark J. Fussa, DO and Sindy M. Paul, MD, MPH, FACPM



On right: buffalo hump photo credit: HIV InSite Knowledge Base <http://hivinsite.ucsf.edu>

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

1. Describe metabolic complications associated with the use of antiretroviral agents.
2. Identify the risks and appropriate management of dyslipidemia for patients on antiretroviral agents.
3. Summarize the treatment of glucose intolerance in patients on antiretroviral agents.
4. Describe lipodystrophy and its management in patients on antiretroviral agents.

Introduction

The medical management of HIV has been revolutionized by the use of highly active antiretroviral therapy (HAART). In the pre-HAART era, HIV typically led to death within ten years. Treatment of HIV with HAART can extend the lifespan of HIV-infected persons by several decades.¹ A major challenge that has arisen out of this success is the management of the side effects of antiretroviral therapy. Antiretroviral therapy (ART) commonly causes various complications, some of which may be life threatening.

This article focuses on some of the more common metabolic complications associated with the treatment of HIV-infected persons, such as dyslipidemia, insulin resistance states, and lipodystrophy syndromes. These abnormalities may eventually lead to an epidemic of cardiovascular disease and diabetes among HIV-infected patients. Management of these complications has therefore become an integral component of HIV care.

HIV causes lipid changes even in the absence of HAART. Low total cholesterol, low high-density lipoprotein cholesterol (HDL), low LDL (low-density lipoprotein), and high triglycerides were commonly seen in the pre-HAART era. Initiation of HAART reverses some of these effects. HDL rises to levels lower than that of the general population. Total cholesterol (including LDL and very-low-density lipoprotein (VLDL)) and triglycerides are all increased by ART. HAART causes an increase of the atherogenic small, dense LDL-2 particle. Of concern is that elevated triglycerides, low HDL, along with small LDL size, comprise the atherogenic dyslipidemia phenotype that is associated with premature atherosclerosis.²

(Continued on next page)

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To obtain continuing education credit for this activity, read the article and complete the quiz, registration and evaluation forms that follow.



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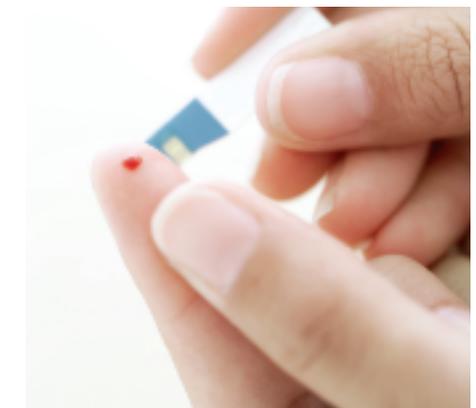
Shortly after HAART was introduced, insulin resistance and occasional frank diabetes were seen. Morphologic changes – lipatrophy and lipoaccumulation – occurred in some patients, particularly those being treated with the NRTI stavudine. In the general population, the pentad of increased abdominal girth, insulin resistance, low HDL, high triglycerides, and hypertension is referred to as the metabolic syndrome.³ The metabolic syndrome is associated with the development of cardiovascular disease and Type 2 diabetes mellitus. Antiretroviral therapy predisposes HIV-infected patients to most of the components of the metabolic syndrome.

A comprehensive approach to the management of HIV-infected patients must take into consideration cardiac and metabolic consequences. A large prospective cohort study demonstrated that HIV-infected patients on HAART suffer cardiac events at an increased rate. The **Data Collection of Adverse Events of Anti-HIV Drugs (D:A:D)** Study Group has followed more than 23,000 HIV-infected individuals to assess whether exposure to antiretroviral therapy increases the incidence of myocardial infarction and other cardiovascular events. Of note, the incidence of traditional risk factors in this relatively young cohort was substantial – 56% had a smoking history, 2.8% were diabetic, 7.2% had high blood pressure, and 45.9% had dyslipidemia. In their initial reporting, 126 patients had had a myocardial infarction (MI) (incidence of 3.5 events per 1000 person-years), 38 patients had a stroke, and 39 patients required cardiac intervention. The incidence of cardiac and cerebrovascular events, including myocardial infarction, increased with increasing exposure to HAART. After adjustment, the relative risk for MI was 1.16%. This leads to a doubling of cardiac risk after five years of exposure to HAART. Overall, the absolute risk of MI remained low, and HAART contributed only partially to the apparent excess risk.^{4,5}

The use of HAART is only one of several factors that contribute to cardiovascular disease in HIV-infected individuals. The following modifiable risk factors for coronary heart disease are targets for risk modification: dyslipidemia, hypertension, cigarette use, diabetes, overweight/obesity (BMI >25/30 kg/m²), inactivity, and atherogenic diet. Older age, male sex, and family history of premature CHD (<55 years

old in a first degree male relative or <65 years old in a first degree female relative) are non-modifiable risk factors.⁶ Other authors have suggested that HIV-infected individuals utilize illicit substances like cocaine and methamphetamine that increase cardiac stress, though this is unproven.⁷ Additionally, interactions between drugs, host, and virus means that metabolic complications are often not the sole consequence of medication.

The D:A:D Study demonstrated that despite the frequent use of lipid lowering agents like statins and fibrates, the risk factor profile among their HIV-infected cohort worsened from 1999 to 2006. This detrimental change in risk factors was partly caused by the aging of the HIV-infected population; as people aged, they also developed diseases like hypertension and diabetes. Over that period of time the incidence of MI remained stable, suggesting that worsening risk factors may have negated the benefits of risk reduction.⁸ Interestingly, the Framingham Cardiac Risk Calculator consistently underestimates the number of events predicted in the D:A:D cohort. This suggests that a lower threshold for intervention (diet, switch, or lipid lowering drugs) should be considered in HIV-infected persons.³



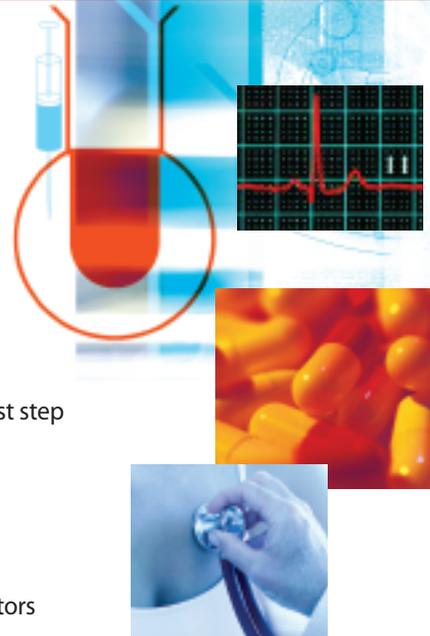
The incidence of traditional risk factors in this relatively young cohort was substantial – 56% had a smoking history, 2.8% were diabetic, 7.2% had high blood pressure, and 45.9% had dyslipidemia. In their initial reporting, 126 patients had had a myocardial infarction (MI) (incidence of 3.5 events per 1000 person-years), 38 patients had a stroke, and 39 patients required cardiac intervention.

Metabolic Complications Associated with the Treatment of HIV-Infected Persons

Management of Dyslipidemia

The National Cholesterol Education Program has produced guidelines, which should be used to guide therapy for dyslipidemia in HIV-infected patients.⁶ The NCEP guidelines were updated in 2004 to provide an option for more aggressive lipid lowering therapy in high risk individuals.⁹ These reports can be accessed at: www.nhlbi.nih.gov/guidelines/cholesterol/index.htm.

- ▶ LDL is the main target of intervention to decrease the risk of CHD. LDL can be calculated as:
 $LDL = \text{total cholesterol} - (\text{HDL} + [\text{triglycerides}/5])$.
- ▶ Determination of an individual's ten-year risk for developing coronary heart disease is an integral first step set forth in the NCEP guidelines. Three strata based on a ten-year risk guide target LDL levels.
 - CHD or CHD equivalents have a >20% risk of experiencing a cardiac event within 10 years. The target LDL is <100 (with an optional target of <70 in very high-risk patients).
 - CHD equivalents are: other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease); diabetes; and multiple risk factors that confer a 10-year risk for CHD >20%.
- ▶ The second category includes patients with 2+ risk factors but a ten-year risk of <20%. The target LDL is <130.
 - In this instance, only age, family history of CHD, smoking history, hypertension, and low HDL cholesterol are applicable.
 - The Framingham Tool is used to calculate 10 year CHD risk. It can be accessed online at <http://hp2010.nhlbihin.net/atp/iii/calculator.asp?usertype=prof>
 - Ten-year Framingham risk is based on age, total cholesterol, HDL cholesterol, gender, smoking history, and systolic blood pressure.
- ▶ The third category includes patients with 0-1 risk factors. They generally have a 10-year risk of <10%. The target LDL is <160. Framingham scoring is not necessary.



The D:A:D Study demonstrated that despite the frequent use of lipid lowering agents like statins and fibrates, the risk factor profile among their HIV-infected cohort worsened from 1999 to 2006. This detrimental change in risk factors was partly caused by the aging of the HIV-infected population; as people aged, they also developed diseases like hypertension and diabetes. Over that period of time the incidence of MI remained stable, suggesting that worsening risk factors may have negated the benefits of risk reduction.⁶



Two main treatment approaches are available to attain NCEP goals for patients on HAART therapy – treatment switching and the addition of lipid lowering agents.

NCEP guidelines recommend that all patients with an elevated LDL be evaluated for remediable secondary causes. These causes include: diabetes mellitus, hypothyroidism, nephrotic syndrome, liver disease, chronic kidney disease, and drugs (including progesterins, steroids, and protease inhibitors).⁹

The LDL treatment goals for HIV-infected individuals are the same as for the general public. In all cases of dyslipidemia, therapeutic lifestyle changes (TLC) should be employed. TLC includes smoking cessation, regular exercise, adhering to a diet high in omega-3 fatty acids, low in total and saturated fats, high in fiber, and fresh fruits and vegetables. If LDL remains above goal after 6 weeks of TLC, intensification is warranted.⁹

Two main treatment approaches are available to attain NCEP goals for patients on HAART therapy – treatment switching and the addition of lipid lowering agents. Several studies suggest that lipid-lowering therapy rarely

attains NCEP goals, and in many instances a combination of drug therapy and switch therapy is required.³

Therapeutic switching is based on the different effects that various antiretrovirals have on cholesterol and triglycerides. Thirty-one antiretroviral agents in various formulations have been approved for the treatment of HIV. Many of these have fallen out of favor and are no longer in routine use. Those which remain fall into one of six classes, each of which may have a different effect on metabolic parameters. Even within a single class, there is variability, for instance, the protease inhibitor ritonavir causes substantial and unfavorable elevations in serum lipids, while the newer protease inhibitor atazanavir has a neutral effect on lipids.³

The D:A:D Study Group compared the risk of MI in patients taking a protease inhibitor-based regimen to those on a non-nucleoside reverse transcriptase inhibitor based regimen.

The incidence of MI increased in both groups through a median of 4.5 years of follow-up. However, the relative rate for patients exposed to PIs was 1.16, which was significant, versus 1.05 (NS) for patients exposed to NNRTIs. Protease inhibitors can cause marked elevations in total cholesterol, LDL cholesterol, and triglycerides. NNRTIs cause more modest increases in total cholesterol, LDL, triglycerides, and HDL.² The questions then become: 1) Do all protease inhibitors have the same effect on lipids? 2) Is it safe and effective to use a PI-sparing regimen?

Among protease inhibitors, ritonavir is associated with the greatest increases in lipids. Both the IAS-USA and the USDHHS guidelines for the treatment of HIV list ritonavir-boosted PIs as recommended treatment options (NNRTIs are also an option in both guidelines; in the USDHHS guidelines alternatives include two unboosted PIs). Obviously exposure to ritonavir happens commonly in the HAART era. Data is pending regarding the effect of lower doses of ritonavir, as used to boost another PI, on lipids are pending. In the AI424-089 study, atazanavir (ATV), a protease inhibitor with a neutral effect on lipids, was examined with and without ritonavir(r). ATV/r was associated with greater increases in total cholesterol and LDL cholesterol than ATV alone. The difference in effect on HDL cholesterol was negligible³. A review of available data shows that of the protease inhibitors, ATV has the smallest impact on lipids, followed by ATV/r. Boosted saquinavir given once or twice daily and boosted fosamprenavir given daily each have a moderate impact on lipids. Lopinavir/ritonavir and twice daily fosamprenavir with ritonavir have the greatest impact among commonly prescribed PIs.³

Research Studies on Safety and Effects Of Highly Effective Antiretroviral Treatment

D:A:D: The Data Collection of Adverse Events of Anti-HIV Drugs Study Group assessed the effect of either a protease inhibitor based regimen or a non-nucleoside reverse transcriptase inhibitor based regimen on the incidence of myocardial infarction and other cardiovascular events.

POWER: Performance Of TMC114/r When evaluated in treatment-Experienced patients with PI Resistance) 1 and 2 (TMC114-C213 and TMC114-C202) studies. In the 24-week primary efficacy analyses, patients receiving one of four darunavir-ritonavir doses plus an optimized background regimen demonstrated better antiviral activity than control PIs (CPIs) in treatment-experienced patients.

SMART: The Strategies for Management of AntiRetroviral Therapy Study Group compared two strategies in nearly 6,000 people worldwide: continuous treatment vs. regularly interrupted treatment (strategic treatment interruption) guided by increases in CD4 counts. The study was stopped early when, despite expectations of benefits in, the data showed that people who interrupted treatment had higher rates of illness and death.

SWAN: The SWitch to ANother Protease Inhibitor study was a 48-week, open-label trial. In patients with virologic suppression who were receiving other PIs, switching to a once-per-day regimen containing atazanavir provided better maintenance of virologic suppression, a comparable safety profile, and improved lipid parameters, compared with those for patients who continued their prior PI-based regimen.

CASE

Management of Hyperlipidemia for Patient on Antiretroviral Agents

Debbie Mohammed, MS, APRN, BC, ACRN, MPH; UMDNJ-University Hospital

JF is a 64-year-old African American male who was diagnosed in October 2000 with HIV infection contracted through heterosexual contact. He has a history of bilateral pneumonia, oral thrush and hypertension managed with Diovan HCT 320/25mg, 1 tablet daily. He has a history of smoking cigarettes in the past; he denies alcohol and illicit drug use. He sees the onsite nutritionist for education regarding his diet regularly and he takes the bus or walks to where he needs to go locally.

TABLE 1
Lipid, GFR, CD4+, VL, and BMI values, 7/02-5/08

Labs	7/02	11/02	3/03	2/04	2/06	8/07	12/07	5/08	Normal Range
Cholesterol	232	227	206	172	218	165		195	(100-200)
Triglycerides	160	97	97	186	93	86		117	(16-200)
LDL	145	133	119	85	105	64		84	(0-130)
HDL	55	75	68	50	94	84		88	>40
GFR mLs/min	>60					49	>60	>60	>60 mLs/min
CD4+	348	360	288	301	470	316	343		689-1600
VL	<400	<400	<400	<400	<400	<50	<50		
BMI	24.3			25.9			25.9		20-25

- In July 2002, JF’s antiretroviral regimen included Agenerase 150 mg po BID with Norvir 100 mg po BID, and Epivir/Ziagen also BID. His total cholesterol level and LDL were noted to be rising. He was started on Pravachol 40 mg orally once/day which was increased 4 months later to 80 mg orally. His cholesterol and LDL levels then began decreasing.
- In February 2004, his regimen was switched to Lexiva 700mg/Norvir 100 mg po BID and Truvada to simplify his medication regimen.
- In February 2006, his cholesterol and LDL were noted to be rising and Zetia 10 mg po OD was started with excellent results noted. However, in August 2007 his GFR was noted to be <49 mLs/min. His HAART was held pending diagnostic studies for kidney disease, which were unremarkable. His GFR spontaneously increased to >60 mLs /min.
- A decision was made in September 2007 to restart HAART, changing regimens using his genotype from June 2001, as the change was due to side effects rather than virologic failure. Mutations included L100L, K103N, G190A/G indicating resistance to NNRTIs. His current regimen is 2 tabs of Prezista 300mg/Norvir 100mg BID, Epzicom 1 tablet po OD, and Fuzeon 90 mg SC BID. Pravachol was discontinued because of the potential for drug interaction with Prezista.
- His GFR has remained >60 mLs/hr. and he is scheduled for a repeat lipid profile with his next set of labwork. His CD4+, HIV viral load and BMI have remained stable over the past six years.
- This patient will continue to require close monitoring of all his lab values.

SWITCHING THERAPY to an atazanavir-based regimen has been assessed. Atazanavir (ATV) is a once daily protease inhibitor that is a recommended component of HAART. ATV can be given either unboosted as a 400 mg dose or as a 300 mg dose boosted with 100 mg of ritonavir. Given the less lipophilic effects of atazanavir, AI424-900 assessed the safety and efficacy of a switch from a more lipophilic protease inhibitor to ATV or ATV/r. Thirty-three treatment-experienced patients with severe dyslipidemia were switched to ATV or ATV/r and followed for 48 weeks. A statistically significant 45.6% decrease in triglycerides and 17.9% decrease in total cholesterol occurred by 24 weeks of therapy, and the change was robust through 48 weeks of atazanavir therapy. Changes in HDL cholesterol and LDL were not statistically significant. After 48 weeks, a re-increase in triglyceride to levels still below baseline was seen while total cholesterol remained lower. The authors noted a coincident increase of patients who were receiving boosted atazanavir at the time, with ritonavir possibly leading to the increase in triglycerides.³

Several studies have examined the effect of replacing PIs altogether. The LipNEFA study was a prospective open-label trial that followed 69 patients who were switched from various PI regimens to a nelfinivir (NFV), efavirenz (EFV), or abacavir (ABC) containing regimen. This study demonstrated a benefit in lipid profiles by switching to a PI-sparing regimen. Seventy percent of enrollees had lipid abnormalities at baseline. Anthropomorphic examinations, lipid levels, and insulin levels were serially followed for 24 months. The ABC arm demonstrated significant decreases in total cholesterol and non-HDL cholesterol. The NNRTI arms had significant improvements in HDL cholesterol, leading to a more cardioprotective TC:HDL ratio. In all 3 treatment arms, triglycerides initially dropped, only to rebound during the second year of the study. The authors point to continued use of stavudine in the backbone as a potential explanation for the triglyceride rebound.¹⁰

Switching therapy may be considered to meet NCEP goals for the management of dyslipidemia. If heavily treatment experienced patients with limited therapeutic options are prescribed switch therapy, careful follow-up must be assured to avoid virologic breakthrough. Planned treatment interruption is not safe, as demonstrated in the SMART Study, a large prospective trial.¹¹

Dyslipidemia may be treated by adding lipid lowering drugs if TLC and switching do not work.¹² A statin should be used to treat isolated hypercholesterolemia. There are many important interactions between antiretroviral agents and statins which can

lead to toxicity. Recommended statins include pravastatin, low-dose atorvastatin, fluvastatin, or rosuvastatin.^{13,14} A fibrate should be used to treat isolated hypertriglyceridemia, typically if the level is in excess of 400 mg/dL. Two fibrates, micronized fenofibrate [Tricor] and gemfibrozil [Lopid] are available. Fish oil also has a significant impact on triglycerides. Both fibrates and fish oil can raise LDL. Niacin can decrease triglycerides and increase HDL, but can also exacerbate insulin resistance. Bile acid sequestrants are relatively contraindicated in HIV because of unknown effects of these agents on the absorption of antiretroviral agents. Ezetimibe is a brush border inhibitor that can lower LDL, especially in combination with statins. In a recent study (ENHANCE), ezetimibe failed to show any improvement in thickness of coronary plaques when paired with simvastatin, as compared to simvastatin alone. However, the combination pill did result in significant reductions in LDL compared with simvastatin alone.¹⁵

Calza compared the addition of lipid lowering agents to switch therapy to see which approach was more effective in improving dyslipidemia. In a randomized, open-label trial, 142 patients with mixed hyperlipidemia on PIs were randomized to receive nevirapine (NVP), efavirenz (EFV), pravastatin, or bezafibrate. At 12 months, decreases in triglycerides, total cholesterol, and LDL were significantly greater with both lipid lowering arms than with the switch arms. At 12 months the proportion of enrollees with normal triglycerides (50.7%) was greater in those on lipid lowering therapy than those who had switched to a PI sparing regimen. Similarly,

the proportion of those with normal LDL by NCEP guidelines was higher after additive therapy (49.2%).¹⁶ It is perhaps important to note that only half of the patients enrolled in the most efficacious arm of this trial attained goals for dyslipidemia. This suggests that a combination of switch therapy and additive therapy may ultimately be necessary to manage dyslipidemia.

Disorders of Glucose Metabolism

Insulin resistance is a risk factor for development of CHD and can lead to the metabolic syndrome and diabetes. Impaired glucose tolerance is defined as either a fasting blood sugar between 100 mg/dL and 125 mg/dL, or a blood sugar of 140 mg/dL to 199 mg/dL two hours after a 75 gram glucose challenge. Diabetes is diagnosed when fasting blood sugar exceeds 126 mg/dL or a two hour glucose challenge test yields blood sugars greater than 200 mg/dL.¹³ Insulin resistance develops when insulin becomes less effective at stimulating target tissues, leading to a hyperinsulinemic state.¹²

The pathogenesis of insulin resistance states is varied. Lipodystrophy syndrome can lead to disorders of glucose metabolism. Among a variety of effects on the glucose metabolic pathways, protease inhibitors can induce insulin resistance through inhibition of peripheral GLUT-4 transporters. As is the case with dyslipidemia, there are variable effects on glucose metabolism within the PI class. Atazanavir and possibly saquinavir have little or no effect on GLUT-4. Lopinavir and indinavir may have short-term effects on insulin sensitivity, but long-term suppression of GLUT-4 is required to markedly alter glucose metabolism. Lopinavir/ritonavir was compared to boosted atazanavir to assess their relative contributions to insulin resistance. Both agents led to some abnormalities in glucose uptake, with lopinavir/ritonavir causing more dysfunctional uptake.³ The clinical significance of this finding is unclear. However, the effect of HAART on glucose metabolism can be striking; impaired glucose tolerance was seen in 35% of HIV-infected patients in one study conducted in 2001; in another study, diabetes was 3.1 times as likely to develop in men receiving HAART for only three years.¹⁷

Metabolic Complications Associated with the Treatment of HIV-Infected Persons

Protease inhibitors and certain NRTIs (especially stavudine) can cause insulin resistance and diabetes. Other risk factors for insulin resistance states include obesity, lipoatrophy, older age, non-Caucasian race, and family history of diabetes.¹³

In the general population, insulin resistance may be present for many before the development of overt diabetes mellitus. Screening for insulin resistance should therefore be a routine part of HIV-patient care. Recommendations are to obtain blood sugars after an 8 to 12 hour fast before the initiation of HIV therapy. Monitoring of fasting blood sugars should occur after any change to the antiretroviral regimen or semi-annually for patients at risk for insulin resistance. A 2-hour glucose tolerance test should be considered for patients with impaired glucose tolerance that is at risk for frank diabetes. The lack of a well defined cutoff means that insulin levels should not be relied on to diagnose insulin resistance.^{12, 13}

Disorders of glucose metabolism can be addressed in several ways. Substitution of a protease inhibitor-based regimen with nevirapine, efavirenz, or abacavir has led to short-term improvements in glucose metabolism and can be considered in the appropriate setting.¹² Generally, the management of glucose abnormalities in HIV-infected patients should be approached as it would be for the general population. Whenever possible, lifestyle modification should be stressed. Other risk factors for the development of CHD should be identified and remedied.

Medications are reserved for patients who have established diabetes. Metformin is a diabetic medication that improves insulin uptake in the periphery. It is unclear whether metformin forestalls the development of diabetes in patients with insulin resistance. Metformin can cause lactic acidosis and should be used cautiously in people receiving an NRTI. It is contraindicated for individuals

with a serum creatinine >1.5. Because it is associated with modest weight reduction, metformin may exacerbate lipoatrophy. Thiazolidenediones (TZDs) improve insulin sensitivity in diabetics and HIV lipodystrophy. Both are known to cause weight gain and fluid retention and recent data suggests they may have detrimental cardiovascular effects. Pioglitazone has been associated with exacerbations of Stage 3 and 4 congestive heart failure. Rosiglitazone has been associated with exacerbations of Stage 3 or 4 CHF and coronary ischemia.¹⁵ These findings should be taken into account in the treatment of HIV-infected persons. Sulfonylureas improve plasma glucose by increasing insulin secretion of pancreatic beta cells. Insulin is effective and inexpensive and may be used to treat diabetes.¹³ Exenatide is an injectable agent for the treatment of Type 2 diabetes that binds to glucagon-like peptide-1 receptors, leading to increased insulin secretion and reduced serum glucose levels. It has not been well studied in HIV-infected individuals.

Lipodystrophy Syndromes

Clinicians and patients began noticing fat distribution abnormalities shortly after the advent of HAART – particularly in regimens that combined NRTIs with protease inhibitors. Lipoaccumulation may occur in the abdomen, dorsocervical fat pad (“buffalo hump”), neck, or breasts. Lipoatrophy involves the loss of subcutaneous fat in the face, extremities, abdomen, or buttocks. In addition to possible negative impacts on lipid profiles and truncal obesity, lipodystrophy may lead to psychological distress. Some patients are reluctant to start or continue antiretroviral therapy because of the body changes that can be encountered. Storage of fatty acids and impaired fatty acid oxygenation in lipodystrophy may lead to hepatic steatosis and insulin resistance.¹⁶ Body fat abnormalities have been reported in 40%-50% of HIV-infected patients and are more common in patients on HAART.

Lipodystrophic changes are apparent in roughly 25% of HIV-infected patients after two years of treatment. Studies of body composition have outlined the mechanisms

by which lipodystrophy occurs. During the first few months of treatment, there is a tendency towards increases in limb fat, followed by a steady decline over years, causing lipoatrophy. Concurrently, truncal fat increases and remains relatively stable for years, possibly leading to truncal obesity (lipoaccumulation).¹⁷

Lipoatrophy is strongly associated with two NRTI/PI regimens. Among NRTIs, the association is particularly strong with stavudine and is more prevalent when stavudine is used in combination with didanosine. NRTIs cause lipoatrophy via inhibition of mitochondrial DNA polymerase. Additional mechanisms by which NRTIs promote lipoatrophy include: inhibition of adipogenesis, inhibition of lipolysis. NRTIs may exert a synergistic toxic effect on adipocytes when used with protease inhibitors.¹⁷ Protease inhibitors are not associated with lipoatrophy when used by themselves.¹³ Additional risk factors for lipoatrophy are older age, nadir CD4+ count <200/ μ L, and lower body weight. Metformin may exacerbate lipoatrophy. Lipoaccumula-

tion is associated with protease inhibitors, but can also occur in patients who are PI-naive. Risk factors for fat accumulation are older age, obesity/higher BMI, caucasian race, and lower nadir CD4+ count.¹³

Screening for lipoatrophy is largely subjective. Clinical trials have used DEXA, CT, and MRI, but the routine use of these modalities as screening tools is hampered by their expense. Objective measures may not be more sensitive than patient reporting and physical exam.

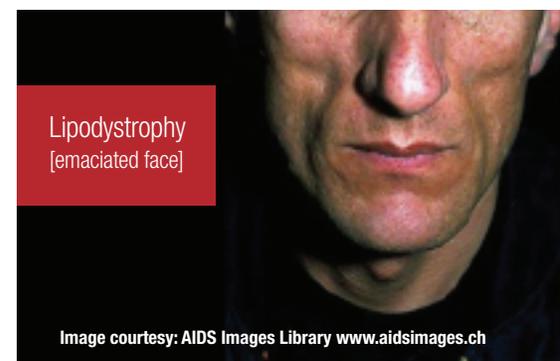


Image courtesy: AIDS Images Library www.aidsimages.ch

There is no objective measure for facial lipoatrophy. Screening for lipoaccumulation can involve anthropomorphic measurements. A waist/hip ratio of >0.85 in women or >0.95 in men is abnormal, as is a waist circumference of >88 cm in women or >102 cm in men. A CT or MRI can detect increases in visceral adipose tissue, but the clinical utility of this finding is often unclear.^{12,13,17}

Several approaches to the management of lipoatrophy are available, but resolution is often disappointingly incomplete. Switch therapy has been investigated. Substituting tenofovir or abacavir for stavudine may lead to modest improvements in lipoatrophy. Modifying therapy from a thymidine-analogue containing regimen to a regimen with abacavir or no NRTIs at all may reverse lipoatrophy. Lopinavir/ritonavir monotherapy may worsen lipids, and

should only be used with caution, if at all. TZDs may increase subcutaneous fat, but studies have yielded mixed results for the treatment of lipoatrophy. Reconstructive procedures may provide substantial cosmetic benefits. Poly(lactic-co-glycolic acid) is FDA approved for the treatment of lipoatrophy, but its use is limited by cost. Other procedures that have been utilized include placement of silicone implants and fat transplantation.^{12,13}

The treatment of lipoaccumulation can be similarly vexing. If obesity is present, it presents an obvious target for intervention through diet and exercise. Metformin has been associated with weight loss and may lead to decreased subcutaneous fat. Studies assessing its use for lipoaccumulation have provided conflicting results. Topical testosterone supplementation may lead to mild-to-modest decreases in subcutaneous abdominal and limb fat. Growth hormone can reduce total fat and visceral fat. Side effects of growth hormone therapy may include insulin resistance. Surgical options include resection of fatty tissue or liposuction, but re-growth of fatty tissue may occur.¹³

CASE

Treatment of glucose intolerance & lipodystrophy in patient on antiretroviral agents

Patricia C. Kloser, MD, MPH

EL is a 55-year-old woman with a family history of diabetes. She was diagnosed with advanced AIDS in 1996, with a CD4⁺ count of 14, and went on her first antiretroviral regimen, Crixivan and Combivir, which she credited with saving her life. Her family had many social and medical problems, contributing to her determination to manage her own care with as little change as possible. However, after about 5 years on the regimen, her weight had increased from 138 to over 200, and she had developed elevated glucose. She was diagnosed with non-insulin-dependent diabetes. She also developed pancreatitis and lipodystrophy.

The physician enlisted the help of a nutritionist to help EL change her diet and manage both the diabetes and pancreatitis. EL was able to lose weight to a healthier 148, though she continues to struggle with this. She also learned when she needed to take medication for her pancreatitis. Her physician finally convinced her that it was dangerous to continue on her old HAART regimen, and she switched to a new regimen, dropping Crixivan because of its effects on her metabolism. The new regimen is Reyataz + Norvir + AZT + 3TC, with a careful dosing schedule to administer epivir three times per week after dialysis, to maintain therapeutic drug levels. Her abnormal lipid profile and diabetes improved.

EL found lipodystrophy very dismaying, as she was working hard to achieve and maintain a healthy weight and figure. She had surgery for her buffalo hump, through a collaboration with a plastic surgeon in another hospital, and was very relieved with the outcome. Her pancreatitis has resolved, and her diabetes has remained under control for several years.

Two years ago, she was admitted to the CCU with a heart attack and developed renal failure, becoming dialysis dependent. She just got her vascular shunt, and now wants to go on the kidney transplant list. She meets the medical criteria for transplant for HIV patients of a CD4+ level over 200 and undetectable VL. Her CD4+ is now >700, and her VL is undetectable.

As her physician, I paused to consider: what is the most amazing thing about this patient?

- That she is still alive, having been diagnosed with HIV in the early 1990s and AIDS in 1996?
- That she was able to lose weight and control her diabetes by diet alone?
- That she is seeking a kidney transplant?
- That she is not depressed despite AIDS, pancreatitis, diabetes, renal failure, lipodystrophy, coronary artery disease, obesity history, and painful low back disease?
- Or—that she was finally convinced to change her HAART to Reyataz, Norvir, AZT, 3TC, when she had already had an undetectable viral load and high CD4+ count?

The greatest challenge was to change her HAART regimen, because EL had managed her HIV care and many co-morbidities through her determination to maintain a full independent life and to make her own decisions. It was difficult for her to believe that the treatment which had saved her life was the cause, in the long run, of many other medical problems.

CASE

Lipodystrophy and its management in patients on antiretroviral agents.

Debbie Mohammed, MS, APRN, BC, ACRN, MPH; UMDNJ-University Hospital

SJ is a 60-year-old man with HIV/AIDS, who was diagnosed in 1995. His risk factor was a blood transfusion. He has a history of opportunistic infections with bartonella, *Pneumocystis jiroveci* (previously known as *Pneumocystis carinii*), and Candida. He has generally been adherent to antiretroviral medications as prescribed since 1995. Not surprisingly, he has a multidrug resistant HIV virus. His current antiretroviral regimen includes: Prezista 300mg with Norvir 100mg orally twice/day, Isentress 400mg po twice daily, Truvada 1 tablet daily and Videx EC 250 mg orally, daily since January 2008. Current CD4+ count is 814 cells (25%), and HIV viral load is <50 copies. His weight is appropriate for his height. He denies smoking, alcohol or illicit drug use and is not sexually active. He has Medicaid and Medicare insurance coverage.



His medical history is significant for hypothyroidism, diabetes mellitus, and hyperlipidemia, depression without suicidal ideation, benign prostatic hypertrophy, GERD and sleep apnea.

In the summer of 2007, SJ attended a support group where he learned about lipodystrophy and became very concerned about his facial appearance. In addition, he reports that he is not sleeping well and feels tired all the time. He reports that his neck hurts when he turns his head from side to side or bends forward.

On physical exam, it was noted that SJ had severe loss of subcutaneous fat in his face, with submental hypertrophy, mild central adiposity, and loss of subcutaneous fat from his arms and legs with prominent veins. He was unable to touch his chin to his neck and able to turn his head only slightly to the sides.

SJ had a surgical evaluation for the submental hypertrophy and was subsequently offered a rhytidectomy with the full support of his psychiatrist. After the surgery, SJ was able to sleep better at night and was less tired during the day. He now has free range of motion to his neck.

However, SJ is still dissatisfied with his facial appearance. He has been referred to a plastic surgeon for possible use of injectable facial filler. He is requesting growth hormone to manage his lipodystrophy. The next steps to resolving his issues are still being evaluated in clinical trials. Hopefully one day soon we may have the answers on the best ways to manage a patient with this side effect to medications.

Consultation with Dr. Kloser:

What can we learn from SJ's history, and what are the next steps? Do you believe that SJ was infected via blood transfusion?

- a. Yes, it is still very common to be infected via blood products.
- b. No, but many people feel more comfortable with this explanation as it "absolves" them of sexual or illicit drug labels.
- c. Yes, he was diagnosed in 1995 and most people who contract HIV via infected blood products live a long time.
- d. No, it is impossible for anyone in a developed country to be infected via blood products.

The most likely answer is b. It may be difficult to have honest discussions with JS about reducing HIV transmission risks.

What could help SJ to improve his self image?

- a. Plastic surgery.
- b. Cosmetic fillers.
- c. Psychotherapy, both group and individual.
- d. Antidepressant medication.
- e. All of the above.

Any or all of these interventions would be helpful to SJ in coping with the metabolic effects of his antiretroviral medications.

Conclusion

With the advent of HAART, it is now possible to durably suppress HIV replication. ♦ Many HIV-infected patients will see their lifespan measured in decades. ♦ In HIV, to prolong life requires uninterrupted therapy with toxic agents. ♦ Unforeseen metabolic consequences of antiretroviral therapy have emerged, creating challenges for clinical management of HIV-infected patients. ♦ Intervention to ameliorate the present and future effects of antiretroviral therapy is necessary to prevent a potential epidemic of cardiac mortality and diabetes in the HIV population. ♦ The management of these complications remains unsettled in many ways. ♦ There is current multidisciplinary research on the metabolic effects of both established and new HIV medications, aimed at further improvements in preventing and managing these potentially fatal side effects.

Metabolic Complications Associated with the Treatment of HIV-Infected Persons

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Metabolic Complications Associated with the Treatment of HIV-Infected Persons

Post-Test

Questions refer to the content of the article and the notes that follow. To receive CME/CE/CEU credit: complete exam, registration, and evaluation forms on-line at www.umdnj.edu/ccoe/aids or fill in the forms on the following pages, and mail or fax to UMDNJ-CCOE (see Registration Form).

- 1. What complications have appeared in HIV positive patients treated with highly active retroviral therapy (HAART)?**
 - A. Decreased subcutaneous fat
 - B. Elevated triglycerides
 - C. Insulin resistance
 - D. All of the above
- 2. Which large cohort study has found that HAART is associated with an increased incidence of myocardial infarction?**
 - A. D:A:D study
 - B. POWER study
 - C. SMART study
 - D. SWAN study
- 3. Which of the following can be used in the management of dyslipidemia in HIV-infected persons?**
 - A. Antioxidant therapy
 - B. Planned holiday from antiretroviral agents
 - C. Substitution of a NNRTI for a PI
 - D. Use of bile acid sequestrants
- 4. What one of the following is a modifiable risk factor for the development of coronary heart disease per NCEP guidelines?**
 - A. Age greater than 70
 - B. High-stress job
 - C. Daily steak and egg breakfast
 - D. Daily alcohol consumption
- 5. Which of the following protease inhibitors is least likely to cause dyslipidemia?**
 - A. Atazanvir
 - B. Fosamprenavir
 - C. Lopinavir
 - D. Ritonavir
- 6. For which of the following medical conditions should a target LDL of less than 100 mg/dL be the goal?**
 - A. Diabetes mellitus
 - B. Elevated HDL cholesterol
 - C. Obesity
 - D. Sleep apnea
- 7. Which of the following HMG-CoA inhibitors (statins) is a preferred agent for the treatment of high cholesterol?**
 - A. Atorvastatin, 80 mg daily
 - B. Pravastatin, 20 mg daily
 - C. Simvastatin, 20 mg daily
 - D. Any of the above
- 8. Which of the following classes of antiretroviral therapy are thought to cause insulin resistance through inhibition of GLUT-4 receptors?**
 - A. Integrase Inhibitors
 - B. Non-nucleoside reverse transcriptase inhibitors
 - C. Nucleoside reverse transcriptase inhibitors
 - D. Protease Inhibitors
- 9. Lipoatrophy is most associated with which of the following antiretroviral agents?**
 - A. Abacavir
 - B. Efavirenz
 - C. Raltegravir
 - D. Stavudine
- 10. Screening for lipid abnormalities should be done:**
 - A. Prior to the initiation of HAART, then every five years.
 - B. Prior to the initiation of HAART, then at least annually.
 - C. Only if the patient is over 21 years of age.
 - D. Only if the patient is on a protease inhibitor containing regimen.

CE Activity Code: 10HC02- DE01



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Metabolic Complications Associated with the Treatment of HIV-Infected Persons *Registration Form*

In order to obtain continuing education credit, participants are required to:

- Read the learning objectives, and review the activity, and complete the post-test.
- Complete this registration form and the activity evaluation form on the next page, and record your test answers below.
- Send the registration and evaluation forms to: UMDNJ-Center for Continuing and Outreach Education
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- Retain a copy of your test answers. Your answer sheet will be graded and if you achieve a passing score of 70% or more, a credit letter awarding 1.25 *AMA PRA Category 1 Credit(s)*TM or 1.25 contact hours or 0.125 continuing education units, and the test answer key will be mailed to you within four (4) weeks.



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Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again.

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POST-TEST <i>Circle the best answer for each question.</i>	1. A B C D	3. A B C D	5. A B C D	7. A B C D	9. A B C D
	2. A B C D	4. A B C D	6. A B C D	8. A B C D	10. A B C D

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Activity Evaluation Form

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants.



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PROGRAM OBJECTIVES: Having completed this activity, are you better able to:		Strongly Agree		Strongly Disagree	
<i>Objective 1:</i>	Describe metabolic complications associated with the use of antiretroviral agents.	5	4	3	2 1
<i>Objective 2:</i>	Identify the risks and appropriate management of dyslipidemia for patients on antiretroviral agents.	5	4	3	2 1
<i>Objective 3:</i>	Summarize the treatment of glucose intolerance in patients on antiretroviral agents.	5	4	3	2 1
<i>Objective 4:</i>	Describe lipodystrophy and its management in patients on antiretroviral agents.	5	4	3	2 1

OVERALL EVALUATION:		Strongly Agree		Strongly Disagree	
The information presented increased my awareness/understanding of the subject.		5	4	3	2 1
The information presented will influence how I practice.		5	4	3	2 1
The information presented will help me improve patient care.		5	4	3	2 1
The faculty demonstrated current knowledge of the subject.		5	4	3	2 1
The program was educationally sound and scientifically balanced.		5	4	3	2 1
The program avoided commercial bias or influence.		5	4	3	2 1
Overall, the program met my expectations.		5	4	3	2 1
I would recommend this program to my colleagues.		5	4	3	2 1

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

Please provide any additional comments pertaining to this activity (positives and negatives) and suggestions for improvement. Please list any topics that you would like to be addressed in future educational activities:

New Legislation for HIV Testing of Pregnant Women and Newborns

(Continued from page 1)

In other words, this law changes the HIV testing of pregnant women in New Jersey from an opt-in system with required written consent or declination as previously required by P.L. 1995, c.174 to opt-out testing. The legislation follows the most recent CDC recommendations for HIV testing of pregnant women.

The new legislation becomes effective 180 days after the Bill was signed into law. The key components of the new legislation are provided below:

- ★ HIV testing of all pregnant women should be part of routine prenatal care.
- ★ Pregnant women should be tested for HIV as early in the pregnancy as possible, and again during the third trimester.
- ★ The physician or health care practitioner shall advise the woman that HIV testing is recommended for all pregnant women as early in pregnancy as possible and during the third trimester and that this testing will be included as part of the routine panel of prenatal tests unless she specifically declines to be tested for HIV.
- ★ Pregnant women who decline HIV testing need to have the declination documented in her medical record.
- ★ A woman shall not be denied appropriate prenatal or medical care because she declines HIV testing.
- ★ HIV testing of all pregnant women shall be voluntary and free of coercion.
- ★ Pregnant women shall not be denied HIV testing on the basis of her economic status.
- ★ A physician or health care practitioner shall provide the woman with information on HIV/AIDS including an explanation of HIV infection, the meanings of positive and negative test results, the benefits of HIV testing as early as possible during pregnancy and again in third trimester, the medical treatment available to treat HIV infection if diagnosed early, the reduced rate of perinatal HIV transmission if she receives HIV treatment, and the interventions available to reduce the risk of mother-to-child HIV transmission.
- ★ The information can be provided orally or in writing. The woman shall be offered an opportunity to ask questions.
- ★ The Commissioner of the New Jersey Department of Health and Senior Services will develop guidelines for the provision of information to the pregnant woman. The Commissioner is also required to establish guidelines regarding notification to a woman of a positive result and to provide, to the maximum extent possible, counseling about the significance of the test result. The regulations need to be consistent with the most recent CDC recommendations.
- ★ A pregnant woman who presents for delivery who has not been tested for HIV during her pregnancy will be given the same information described above as soon as it is medically appropriate, and she should be tested for HIV as soon as medically appropriate, unless she declines HIV testing after provided with the information.
- ★ If the HIV status of the mother of the newborn is unknown, each birthing facility in New Jersey will be required to test the newborn for HIV.
- ★ The newborn shall not be denied HIV testing on the basis of its economic status.
- ★ The Commissioner of the New Jersey Department of Health and Senior Services will establish a comprehensive program for follow-up testing of newborns that test positive for HIV or whose mother is HIV positive. This needs to include at least procedures for administering the HIV testing, counseling the mother, tracking the newborn, disclosure of the newborn's HIV test results to the mother, facility compliance reviews, and educational activities related to the HIV testing.



- ★ The provisions shall not apply to a newborn whose parents object to the test as being in conflict with their religious tenets and practices. A written statement provided by the parents of the objection needs to be included in the newborn's medical record.

This issue of AIDSLine provides additional information on the epidemiology of perinatal HIV transmission in New Jersey and the most recent medical recommendations for the maximal reduction of perinatal HIV transmission. The NJDHSS, DHAS, is planning a perinatal conference for the fall of 2008. In addition, the NJDHSS, DHAS provides a continuing medical education lecture on reducing the risk of vertical HIV transmission.

Inquiries regarding this lecture and the fall 2008 perinatal HIV prevention conference should be addressed to: Michelle Thompson, University of Medicine and Dentistry of New Jersey-Center for Continuing and Outreach Education, Division of AIDS Education, at (973) 972-1293 or ccthomps@umdnj.edu. NJDHSS, DHAS is also collaborating with the Francois Xavier Bagnoud Center (FXBC) at the University of Medicine and Dentistry of New Jersey to provide informational and technical assistance to physicians, providers, and facilities. For more information or assistance contact Elaine Gross at (973) 972-5324 or grossej@umdnj.edu.

REFERENCES

1. Centers for Disease Control and Prevention. Revised Recommendations for HIV Testing of Adults, Adolescents and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(RR14):1-1.
2. Centers for Disease Control and Prevention. Rapid HIV Antibody Testing During Labor and Delivery for Women of Unknown HIV Status: A Practical Guide and Model. 2004 http://www.cdc.gov/hiv/rapid_testing/materials/Labor&DeliveryRapidTesting.pdf

USDHHS Guidelines

Updated Guidelines on Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis

Guidelines for managing pharmacologic interactions that can result when patients receive antiretroviral drugs for treatment of human immunodeficiency virus (HIV) infection together with rifamycins for treatment of tuberculosis have been published previously (1--3). Updated guidelines, with recommendations from CDC and its partners, are now available at http://www.cdc.gov/tb/tb_hiv_drugs/default.htm.



The updated guidelines include recommendations for use of newer antiretroviral drugs, including those in new classes, such as CCR5 receptor antagonists and integrase inhibitors. The new guidelines provide additional recommendations regarding use of rifampin with antiretroviral therapy; these recommendations are critical in regions where rifabutin is unavailable. Changes from previous versions of these guidelines include 1) summaries of clinical experience with use of specific antiretroviral regimens during tuberculosis treatment (in addition to pharmacokinetic data), 2) a table summarizing clinical experience with key antiretroviral regimens and providing recommended regimens, and 3) sections on treatment for special populations (i.e., young children, pregnant women, and patients with drug-resistant tuberculosis). The online guidelines will be updated periodically to provide clinicians with the latest information.

References

1. CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998;47(No. RR-20).
2. CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2000;49:185--9.
3. CDC. Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2004;53:37. Reprinted from 2/1/08 *MMWR*, Notice to Readers

Guidelines for the Use of Antiretroviral Agents

The Panel on Antiretroviral Guidelines for Adult and Adolescents has released another update to the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents as of January 29, 2008.

<http://aidsinfo.nih.gov/Contentfiles/AdultandAdolescentGL.pdf>

Regimens for Initial Therapy:

The Panel revised its recommendations for several "preferred" and "alternative" antiretroviral components for treatment-naïve patients, significantly:

- Abacavir + lamivudine has been changed from "alternative" to "preferred" 2-NRTI component in patients who have tested negative for HLA-B*5701 (All).
- Zidovudine + lamivudine has been changed from "preferred" to "alternative" 2-NRTI component (BII).

Other Updated Sections:

- Treatment Interruptions
- Acute Infections
- TB Coinfection with HIV

Reprinted from: AETC National Resource Center Monthly Update, February 2008 <http://www.aidsinfo.org>

Conference Reports Podcast and Videocast: CROI

Weblink: http://www.retroconference.org/2008/data/files/retro2008_frameset.htm

Note: Podcasts and videocast are now available for many of the sessions at The Conference on Retroviruses and Opportunistic Infections (CROI) from February 3-6, 2008 in Boston.

FDA: Drug Cautions

UNITED STATES: "FDA Alerts Doctors to Johnson & Johnson's HIV Drug's Possible Link to Liver Damage, Deaths" Associated Press (03/21/08)

On Friday, US health officials warned doctors that Johnson & Johnson's HIV drug Prezista could be linked to liver illness and death in some patients. Original studies found that 0.5% of patients taking Prezista developed drug-induced hepatitis, the new Food and Drug Administration-approved labeling for Prezista states. Since the drug's 2006 approval, FDA says it has received more reports of hepatitis, some fatal, mostly in patients with advanced HIV who took many medications.

For more information, visit

www.fda.gov/cder/drug/infopage/darunavir/default.htm

CDC announces HIV/AIDS Web Series

The CDC announced that it is ending its HIV/AIDS Satellite Broadcast Program and launching a web-based program. The first in this series will be "A Call to Action for Leaders: The Crisis of HIV/AIDS among African Americans." Parts 1-3 will be 30-minute segments available beginning June 30, 2008, from the Public Health Training Network, at <http://www2a.cdc.gov/phtn>. Parts 4-6 will be available November 30, 2008.

A Call to Action for Leaders:

The Crisis of HIV/AIDS among African Americans

June 30, 2008 – Parts 1-3

November 30, 2008 – Parts 4-6

This Web series may be viewed online.

For more information, visit

<http://www.cdcnpin-broadcast.org/>
or call 800-458-5231.

National HIV/AIDS TREATMENT RESOURCES: Guidelines, Statistics, And Clinician Consultation

Centers for Disease Control (CDC) – Division of HIV/AIDS Prevention

HIV/AIDS research, surveillance reports, funding announcements, research and reporting software, epidemiology slide sets

<http://www.cdc.gov/hiv/hivinfo.htm#WWW>

Rapid Testing: http://www.cdc.gov/hiv/rapid_testing

MMWR [Morbidity and Mortality Weekly reports]:

<http://www.cdc.gov/hiv/pubs/mmwr.htm>

CDC National Prevention Information Network (NPIN)

HIV, STD, and TB news, funding, materials, conference calendars.

<http://www.cdcnpin.org>

US Dept. of Health & Human Services

www.aidsinfo.nih.gov • 1-800-HIV-0440 (1-800-448-0440)

HIV/AIDS treatment guidelines; prevention, treatment, and research.

National Institutes of Health-sponsored searchable

clinical trials database: <http://clinicaltrials.gov>

FDA MedWatch

Updated reports on medication interactions and warnings:

1-800-FDA-1088; Subscribe to e-bulletin:

<http://www.fda.gov/medwatch/elist.htm>

National HIV/AIDS Clinicians' Consultation Center

<http://www.nccc.ucsf.edu>

Consultation on antiretroviral therapy, drug resistance, opportunistic infection prophylaxis and treatment, laboratory evaluation; occupational exposure, perinatal intervention.

Warmline: 800-933-3413

National Clinicians' Post-Exposure Prophylaxis Hotline

(PEpline): 888-448-4911 (888-HIV-4911)

National Perinatal HIV Consultation and Referral Service

888-448-8765 (888-HIV-8765)

Ryan White Planning and Coordination Bodies in New Jersey

Ryan White Part A

New Jersey HIV/AIDS Community Planning Group Rutgers, The State University of New Jersey

3 Rutgers Plaza, 2nd Floor
New Brunswick, NJ 08901

Tel: 732-932-3358 x2006 • Fax: 732-932-3357

Website: <http://hpcpsdi.rutgers.edu>

Newark EMA Health Services Planning Council (Essex, Union, Morris, Sussex & Warren Counties)

315 North 6th Street, 2nd Floor
P.O. Box 7007, Newark, NJ 07107

Tel: 973-485-5220 • Fax: (973) 485-5085

Website: www.newarkema.org

Hudson County HIV Health Services Planning Council

574 Summit Avenue, 5th Floor
Jersey City, NJ 07036

Tel: 201-795-4555, ext. 212 • Fax: (201) 795-0204

Contact: Marvin Krieger, Planning Council Chairperson

Email: HcHIVcncl@aol.com

Paterson-Passaic County-Bergen County HIV Health Services Planning Council

c/o Buddies of NJ, Inc.
149 Hudson Street

Hackensack, NJ 07601

Contact: Steven Scheuerman, Planning Council Chairperson

Tel: 201-489-2900

Website: www.aidsnj.org

Ryan White Part A

Middlesex, Somerset, Hunterdon HIV Health Services Planning Council

Institute for Families, Rutgers University
100 Joyce Kilmer Avenue

Piscataway, NJ 08854

Contact: David Williams

Tel: 732-445-0512 • Fax: (732) 445-4154

Email: dwilliams@ssw.rutgers.edu

Website: www.mshema.org

Philadelphia EMA Ryan White Part A Planning Council

340 N. 12th St., Suite 203
Philadelphia, PA 190117

Tel: 215-574-6760, ext. 104 • Fax: (215) 574-6761

Website: www.hivphilly.org

(includes Camden, Salem, Cumberland Counties in NJ)

Cumberland County HIV Services Planning Council

790 East Commerce Street
Bridgeton, NJ 08302

Tel: 800-870-0568 • Fax: 609-927-7361

Ryan White Part B

New Jersey Department of Health & Senior Services Division of HIV/AIDS Services – Care & Treatment Unit

PO Box 363, Trenton, NJ 08625

Phone: 609-984-6328 • Fax: 609-292-6009

Hotline: 1-800-624-2377

Website: <http://www.state.nj.us/health/aids>

New Jersey Department of Health & Senior Services – Division of HIV/AIDS Services (DHAS)

New web address: <http://www.state.nj.us/health/aids>

- **NJ HIV/AIDS Semi-annual Newsletter** (statistical report); policies, and guidelines for HIV/AIDS care and services in New Jersey
- **New Jersey rapid testing site:** www.state.nj.us/health/aids/rapidtesting
- **New Jersey HIV (Testing) Helpline:** 1-866-HIV-CHEC
- **New Jersey AIDS/STD Hotline:** (800) 624-2377
–24-hour professionally-staffed service –Consultation, testing referrals, free materials

**New Jersey HIV (Testing) Helpline:
1-866-HIV-CHEC**

HIV/AIDS TRAINING & EDUCATION

Sponsors: Division of AIDS Education at UMDNJ-Center for Continuing and Outreach Education with funding from the NJ Department of Health & Senior Services, Division of HIV/AIDS Services.



HIV/AIDS Medical Update Series – FREE ON-SITE TRAINING

To schedule a free 1-hour HIV medical education program at your health care site on any of these topics, contact Michelle Thompson at (973) 972-1293 or ccthomps@umdnj.edu

- Diagnosis and Initial Management of HIV/AIDS: What the Primary Care Physician Should Know
- HIV in Pregnancy – Preventing Perinatal Transmission
- HIV/AIDS and Hepatitis C Co-Infection
- Immunizations for HIV Positive Adults
- Non-Occupational Post-Exposure Prophylaxis
- Prevention and Prophylaxis for Occupational Exposure to HIV and Other Blood Borne Pathogens
- Prophylaxis and Treatment of Opportunistic Infections in Patients with HIV Disease
- Rapid Diagnostic HIV Testing

University of Medicine & Dentistry of NJ Center for Continuing & Outreach Education – Division of AIDS Education

www.umdnj.edu/ccoe/aids

Conferences, training for HIV/AIDS health and social service professionals.

Free online CME/CE – topics include:

Video/Slides: HIV Clinical Update 2007:

- HIV Treatment and Research Update
- Hepatitis B and HIV Co-Management
- Street Drugs, OTCs and HIV Medications

Articles:

- Role of Newly Approved HIV Antiretroviral Agents in Treatment-Experienced Patients
- Medical Implications of Injection Drug Use
- HIV Treatment Update
- Contraindicated Medications and Regimens for HIV-Infected Patients
- Immunization for HIV Infected Children and Adolescents
- Prevention & Treatment of HIV Infection in Persons 50 & Over
- Perinatal HIV Prevention and the 2007 New Jersey Legislation
- Metabolic Complications Associated with the Treatment of HIV-Infected Persons

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Division of HIV/AIDS Services



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SAVE THE DATES

October 14, 2008

Reducing Mother-to-Child HIV Transmission in New Jersey

New Jersey Hospital Association Conference Center • Princeton, NJ

*This conference is sponsored by UMDNJ-CCOE and the
New Jersey Department of Health and Senior Services, Division of HIV/AIDS Services.
www.umdj.edu/ccoe/aids • (973) 972-3690*

See page 16 for further information on conference including poster session.

December 10, 2008

19th Annual HIV Medical Update

Crowne Plaza • Cherry Hill, NJ

*Sponsored by UMDNJ-CCOE and
the New York/New Jersey AIDS Education & Training Center
www.umdj.edu/ccoe/aids • (973) 972-3690*

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