NEW JERSEY AIDS Line

January 2009

Published by UMDNJ-Center for Continuing & Outreach Education, Division of AIDS Education

Prior Authorization Required for Second Line HIV Medications in New Jersey

Sindy M. Paul, MD, MPH, FACPM; Ronald Weinstein, MBA; and Martin T. Zanna, MD, MPH; New Jersey Department of Health Health & Senior Services, Division of HIV/AIDS Services; Sam Emenike, PharmD; and Barbara Haas, RPh; UNISYS

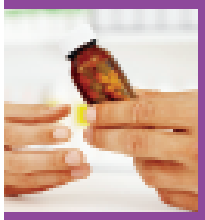
IN THE EARLY 1980S WHEN THE HIV/AIDS EPIDEMIC BEGAN, people with AIDS were not likely to live longer than a few years.[1] There were no effective treatments, and the first antiretroviral agent did not become available until zidovudine (ZDV) was approved by the Food and Drug Administration (FDA) in 1987. Today, there are 32 FDA-approved antiretroviral agents, in five major classes.[2] With the development of safe and effective combination antiretroviral therapy, most people infected with HIV now have longer and healthier lives. Although these medications can suppress the virus, even to undetectable levels, they do not cure HIV/AIDS.[1] While patients are on antiretroviral agents, the virus can develop resistance to the medications.

The five classes of antiretroviral agents currently approved by the FDA are described below.

1. ***Reverse transcriptase (RT) inhibitors*** interfere with the critical step during the HIV life cycle known as reverse transcription. It is during this step that RT, an HIV enzyme, converts HIV RNA to HIV DNA. There are two main types of RT inhibitors.
   - *Nucleoside/nucleotide RT inhibitors* are faulty DNA building blocks. When these faulty pieces are incorporated into the HIV DNA (during the process when the HIV RNA is converted to HIV DNA), the DNA chain cannot be completed, thereby blocking HIV from replicating in a cell.
   - *Non-nucleoside RT inhibitors* bind to RT, interfering with its ability to convert the HIV RNA into HIV DNA.[1]
2. ***Protease inhibitors*** interfere with the protease enzyme that HIV uses to produce infectious viral particles.[1]
3. ***Entry and fusion inhibitors*** interfere with the virus' ability to fuse with the cellular membrane, thereby blocking entry into the host cell.[1]
4. ***Integrase inhibitors*** block integrase, the enzyme HIV uses to integrate genetic material of the virus into its target host cell.[1]
5. ***Multidrug combination products*** combine drugs from more than one class into a single product.[1]

(Continued on page 29)

2nd Line/Salvage HIV Medications



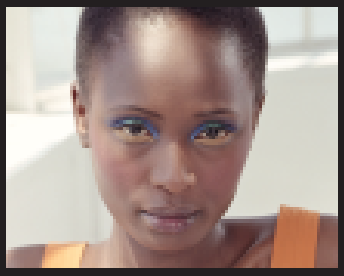
- Enfuvirtide (Fuzeon)
- Etravirine (Intelence)
- Maraviroc (Selzentry)
- Raltegravir (Isentress)
- Tipranavir (Aptivus)

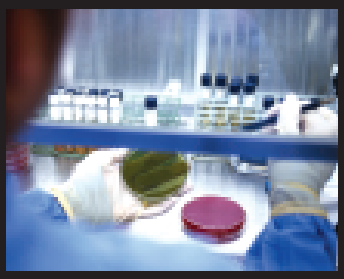
PRIOR AUTHORIZATION IS REQUIRED

- Beneficiary Comes to Pharmacy with Prescription
- Pharmacist Reviews Beneficiary's Drug Profile
- Pharmacist Calls Medical Exception Program (MEP) – Provides Information to MEP
- MEP Initiates Paperless PA Process
- If necessary, MEP Calls Physician/ Prescriber to obtain Clinical Information to Approve or Deny
- MEP Calls Back Pharmacist To Communicate Outcome of PA Process
- PA is either approved or denied
- If PA is approved, medication is dispensed.

Published by UMDNJ-Center for Continuing & Outreach Education, Division of AIDS Education with the New Jersey Department of Health and Senior Services, Division of HIV/AIDS Services

CE Continuing Education





News Feature

Resources

Save the Date

June 11, 2009
HIV Clinical Update
Sheraton at Woodbridge Center
Iselin, NJ
(see back page)

Women and HIV Treatment: Recently Reported Data

Release Date: January 2009 • Expiration Date: June 30, 2010 • Course Code: 11HC03-DE01
Nursing Credit for this activity will be provided through June 30, 2010.

Sponsor
Sponsored by the University of Medicine and Dentistry of New Jersey (UMDNJ), Center for Continuing and 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 women and/or persons with HIV/AIDS.

Statement of Need
Since the beginning of the HIV/AIDS epidemic, researchers, clinicians, patients and advocates have raised concerns about whether women with HIV infection have different disease manifestations or response to treatments. Women with HIV/AIDS are now included in almost all clinical trials of HIV treatments, although there are often restrictions related to protection of women and fetuses, for women of child-bearing age. The USDHSS HIV treatment guidelines published in January 2008 included a section titled "Considerations For Antiretroviral Use In Special Patient Populations: HIV-Infected Women of Reproductive Age and Pregnant Women."[1] Updated guidelines published in November 2008, referenced in this article, continue the previous specific recommendations for treatment of women.[2]

[1] Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 29, 2008; 1-128. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

[2] Guidelines for the use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents, Department of Health and Human Services, November 3rd. 2008. Available at: http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf.

Learning Objectives
Upon the completion of this activity, participants should be able to:
1) Summarize the epidemiology of HIV infection in US women
2) Identify antiretroviral drug interactions with oral contraceptives and changes in pharmacokinetics that may occur with antiretroviral dosing in pregnancy
3) Describe recent antiretroviral clinical trial results, including comparison of outcomes among men and women.

Activity Director(s)/CME Academic Advisor(s)
• Patricia Kloser, MD, MPH, UMDNJ-NJ Medical School

Planning Committee
• Sindy Paul, MD, MPH, FACPM, New Jersey Dept. of Health and Senior Services
• Debbie Y. Mohammed, MS, MPH, APRN-BC, UMDNJ-University Hospital
• Linda Berezny, RN, BA, New Jersey Dept. of Health and Senior Services
• Kimi Nakata, MSW, MPH, UMDNJ-CCOE

Faculty
Sally Hodder, MD, is Professor of Medicine, Vice Chair and Director of HIV Programs, Department of Medicine, New Jersey Medical School, University of Medicine and Dentistry of New Jersey. She previously served as the Vice President of U.S. Virology Medical Affairs at Bristol Myer Squibb. Dr. Hodder is a frequent contributor to Clinical Care Options webcasts and other medical education activities. She presented a poster on clinician provision of reproduction counseling to HIV-infected women at the 2008 International AIDS Conference in Mexico City.

Method of Instruction
Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the self-assessment test which consists of a series of multiple-choice questions. Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a credit letter and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials; or may complete the activity on the internet at www.umdnj.edu/ccoe. Estimated time to complete this activity as designed is 1.25 hours.

Accreditation
Physicians: UMDNJ-Center for Continuing and Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. UMDNJ-Center for Continuing and Outreach Education designates this educational activity for a maximum of 1.25 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nurses: The University of Medicine and Dentistry of New Jersey-Continuing Education and Outreach Education is an approved provider of continuing nursing education by the New Jersey State Nurses Association, Provider Number P173-10/06-09. New Jersey State Nurses Association is accredited by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is awarded 1.25 contact hours.

UMDNJ-Center for Continuing and Outreach Education is an approved provider of continuing education by the California Board of Registered Nursing, Provider Number CEP 13780 for a maximum of 1.25 contact hours for this activity.

Review: This activity was peer reviewed for relevance, accuracy of content, and balance of presentation by Patricia Kloser, MD, MPH; Debbie Y. Mohammed, MS, MPH, APRN-BC, and Brenda Christian, MEd, PA-C; and pilot tested for relevance and time required for participation by Kinshasa Morton, MD; Bonnie Abedini, MSN, RN; Mary C. Krug, RN, MSN, APN-C; and Kara Winslow, BSN, RN.

Faculty Disclosure Declarations
Dr. Hodder has disclosed the following: She was on the speaker's bureau of BMS, has received grant/research support from BMS, Gilead, Tibotec and Pfizer; has been a consultant on advisory boards for: BMS, Gilead, Tibotec, and Boehringer-Ingelheim; and is a shareholder of Merck. Debbie Mohammed has disclosed the following: she is on the speaker's bureaus of BMS and Gilead.

Conflicts of interest were resolved by review by Activity Director Patricia Kloser, MD, MPH.

The following have no financial relationships to disclose: Activity Director Patricia Kloser, MD, MPH; Planning committee members Sindy M. Paul, MD, MPH, FACPM; Linda Berezny, RN, BA; and Kimi Nakata, MSW, MPH (editor); content reviewer Brenda Christian, MEd, PA-C; and field testers: Kinshasa Morton, MD; Bonnie Abedini, MSN, RN; Mary C. Krug, RN, MSN, APN-C; and Kara Winslow, BSN, RN.

Off-Label Usage Disclosure
This activity contains information about commercial products that are unlabeled for use or investigational uses of products not yet approved: Vicriviroc is currently in Phase II/III clinical trials. Darunavir is in FDA Pregnancy Category B, and lopinavir/r is in FDA Pregnancy Category C; each should be used only if the potential benefit justifies the potential risk.

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.

Women and HIV Treatment: Recently Reported Data

Sally L. Hodder MD, Professor of Medicine, New Jersey Medical School, Newark, New Jersey

LEARNING OBJECTIVES

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

1. Summarize the **EPIDEMIOLOGY** of HIV infection in US women.
2. Identify antiretroviral **DRUG INTERACTIONS** with **ORAL CONTRACEPTIVES** and changes in **PHARMACOKINETICS** that may occur with antiretroviral **DOSING IN PREGNANCY**.
3. Describe recent **ANTIRETROVIRAL CLINICAL TRIAL RESULTS**, including **COMPARISON** of outcomes among **MEN & WOMEN**.

(Continued on next page)

Release Date: January 2009 • Expiration Date: June 30, 2010 • Course Code: 11HC03-DE01 • Nursing Credit for this activity will be provided through June 30, 2010.

To obtain continuing education credit, complete the quiz, registration, and evaluation on the following pages, or go to: www.umdnj.edu/ccoe/aids

Sally Hodder, MD, is Professor of Medicine , Vice Chair and Director of HIV Programs, Department of Medicine, New Jersey Medical School, University of Medicine and Dentistry of New Jersey. She previously served as the Vice President of U.S. Virology Medical Affairs at Bristol Myer Squibb. Dr. Hodder is a frequent contributor to Clinical Care Options webcasts and other medical education activities. She presented a poster on clinician provision of reproduction counseling to HIV-infected women at the 2008 International AIDS Conference in Mexico City.

Sponsored by the University of Medicine & Dentistry of New Jersey (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.

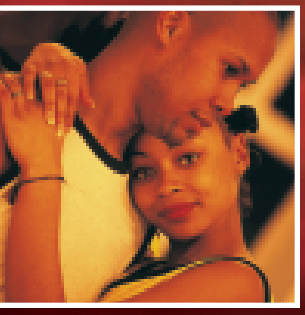
Case No. 1

Ms. J. is a 47-year-old Black woman who presents with fever, oral ulcers, pharyngitis, and cervical lymphadenopathy. Work-up to date is negative, though Ms. J. elected to opt out of HIV testing because she feels that she is not at risk. She states that she has never used illicit drugs of any sort and has had a monogamous sexual partner (though he never uses condoms). After further discussion, Ms. J. agrees to HIV testing and is found to have a positive rapid test and an indeterminate Western Blot.

COMMENT: Though Ms. J. presents with symptoms suggestive of acute retroviral syndrome, these symptoms are also consistent with a number of other diagnoses. In a prospective cohort study, Hecht et. al found that fever (Odds ratio 5.2; 95% CI 2.3-11.7) and rash (Odds ratio 4.8; 95% CI 2.4-9.8) were strongly associated, by multivariate analysis, with the presence of acute retroviral infection.[1] The Western Blot should be repeated in several weeks, and HIV RNA testing may be helpful in defining likely presence of HIV infection.

The CDC recently estimated that:

- 56,300 HIV new infections occur annually in the U.S., a more accurate estimate than previous approximations of 40,000 annual new U.S. infections.[2]
- Noteworthy is that 27% of U.S. infections now occur in women,[3] an increase from 20 years ago. Black women are disproportionately affected, constituting 66% of US women with HIV infection in 2005, but only 13% of the US female population.[4,5]
- Many women perceive themselves to be at "low risk" for HIV infection as does Ms. J. In a survey of obstetricians and gynecologists, Gray, et al. reported that the major reason women decline HIV testing is that they reportedly believe themselves to be at low risk for HIV acquisition.[6]
- Black women without high risk behaviors may be at increased risk for HIV acquisition compared with their white counterparts.
- Hallfors, et al., in a study population of 8,706 non-Latino blacks and whites 18-26 years of age, found that in a subgroup of individuals with low risk behaviors, both Black men and women were 25 times more likely than their white counterparts to acquire a sexually transmitted infection (STI) and/or HIV infection. These data suggest that the risk of STI and HIV infection is not only associated with their behaviors but also with the risk behaviors of their partners or other unmeasured factors.[7]



Black men and women were 25 times more likely than their white counterparts to acquire a sexually transmitted infection (STI) and/or HIV infection. These data suggest that the risk of STI and HIV infection is not only associated with their behaviors but also with the risk behaviors of their partners or other unmeasured factors.[7]

THE CDC RECENTLY ESTIMATED THAT

56,300 HIV new infections occur annually in the U.S., a more accurate estimate than previous approximations of 40,000 annual new U.S. infections.[2]

Noteworthy is that 27% of U.S. infections now occur in women[3] an increase from 20 years ago.

Black women are disproportionately affected, constituting 66% of US women with HIV infection in 2005, but only 13% of the US female population.[4,5]

Case No. 2

Ms. L. is a 33-year-old woman who comes to your office for routine HIV follow-up. She has been aware of her HIV infection for the past year and has been followed at another clinic. She advises you that she has never had any opportunistic infections; however, she has been told that she should consider starting antiretroviral therapy. Physical examination is normal, her most recent $CD4^+$ count is 320 cells/mm,^{3} and her HIV RNA viral load is 110,000 copies/ml. You and she decide that it is time to start antiretroviral therapy. ***Which of the following do you choose?***

A **Efavirenz + zidovudine/lamivudine** as a fixed dose combination because current data suggest that efficacy is better than the alternatives.

B **Efavirenz/tenofovir/emtricitabine** as a fixed dose combination because recent data indicate that time to virologic failure is longer with this combination compared with alternatives.

C **Lopinavir/ritonavir (fixed dose combination) + abacavir/lamivudine** because the incidence of lipoatrophy is less than with efavirenz-based regimens.

D **Darunavir + ritonavir + tenofovir/emtricitabine** because recent 96-week trial data in antiretroviral naïve patients demonstrate superiority to lopinavir/ritonavir-based therapy.

E **Further discussion with the patient** to determine her toxicity concerns regarding antiretroviral therapy as well as her reproductive needs.

Efavirenz (EFV), a component of regimens in answers A and B, is classified as an FDA Pregnancy Category Class D drug; animal data show an increased risk of central nervous system (CNS) defects and there have been several retrospective reports of CNS defects in infants exposed to efavirenz.[10] As the neural tube forms in the first month of pregnancy, EFV should not be used in women of child-bearing potential unless a barrier form of contraception as well as another method of contraception (e.g., hormonal contraception) are consistently used. In addition, a negative pregnancy test result should always be documented before initiation of EFV. Tenofovir/emtricitabine combined with efavirenz has been demonstrated to have superior durability of virologic control as well as an improved safety profile compared with zidovudine/lamivudine combined with efavirenz,[11] and less lipoatrophy has been reported with lopinavir/ritonavir-containing regimens when compared to efavirenz regimens.[12] Noteworthy, is that the November 3, 2008 Department of Health and Human Services (DHHS) Guidelines continue to recommend tenofovir with either lamivudine or emtricitabine as the preferred nucleoside reverse transcriptase inhibitor (NRTI) backbone.[13]

The combination of Abacavir + lamivudine was recently moved from *preferred to alternative NRTI status* in the DHHS guidelines for two reasons:

1) IN ACTG (AIDS Clinical Trials Group) 5202, a large randomized study in treatment naïve persons comparing tenofovir/emtricitabine to abacavir/lamivudine when used in combination with either efavirenz or with atazanavir/ritonavir, the Data Safety Monitoring Board (DSMB) recommended termination of the study in participants with starting viral loads ≥100,000 copies/ml, as data demonstrated a shorter time to virologic failure if they had been randomized to abacavir/lamivudine (ABC/3TC) compared to individuals randomized to tenofovir/emtricitabine (TDF/FTC).[14] Participants with starting viral loads <100,000 copies/ml remain on study. It is noteworty that 96-week data from a smaller study (the HEAT Study) comparing ABC/3TC to TDF/FTC, each in combination with lopinavir/ritonavir, did not demonstrate significant differences in the proportion of virologically suppressed patients with starting viral loads ≥100,000 copies/ml among participants randomized to the two arms.[15]

2) TWO STUDIES have indicated an increased incidence of myocardial infarction among patients currently (or within six months) of taking abacavir.[16,17] Though a pooled analysis of clinical trials involving 9,639 patients taking abacavir (compared with 5,044 participants not taking abacavir) did not reveal an elevated risk of myocardial infarction,[18] the guidelines committee concluded that ABC/3TC should be used with caution in patients with HIV RNA viral loads >100,000 copies/ml or with increased cardiovascular risk.[13] Ritonavir boosted darunavir with tenofovir/emtricitabine has been shown to be superior to lopinavir/ritonavir + tenofovir/emtricitabine.[19] However, there are scant data on use of darunavir in pregnant women. It is noteworthy that ritonavir-boosted darunavir was designated as a "preferred" protease inhibitor in the most recent DHHS guidelines.[13]

(Continued on next page)

Multiple presentations at recent conferences have addressed issues of women living with HIV. The Women Living Positive survey, an anonymous phone interview of 700 HIV-infected women (43% Black, 29% Latino, and 29% Caucasian) who had lived with HIV infection a mean of 10.6 years (8.1 years on antiretroviral therapy), found that nearly half (48%) of the survey respondents were never asked by their health care provider about their current or future childbearing plans.[20] Clearly, HIV care providers are missing important opportunities to discuss contraception and preconceptive care, particularly as relates to antiretroviral treatment. As highlighted in the above case presentation, an important factor in antiretroviral agent selection is the reproductive intention of the patient.

Antiretroviral agents may have a wide range of effects on oral contraceptive hormone levels.

A study of the interaction of oral contraceptives agents with vicriviroc or SCH-D (a new CCR5 antagonist in development) demonstrated no significant interaction per se with vicriviroc.[21] Another recently reported study of women given oral contraceptives and efavirenz, presented at the 2008 ICAAC/IDSA conference in Washington DC, demonstrated that ethinyl estradiol levels were not altered, however, norelgestromin, a metabolite of progestin as well as levonorgestrel (an active component of some oral contraceptive agents) were decreased.[22] Therefore, a barrier contraceptive is recommended in addition to oral contraceptive agents in women taking efavirenz to assure effective contraception as well as effective protection against HIV transmission. Studies of protease inhibitors' effects on levels of oral contraceptives have demonstrated decreased ethinyl estradiol levels with ritonavir[21] and lopinavir/ritonavir,[23] but increased levels with atazanavir.[24]

By and large, levels of antiretroviral agents are in most cases unaffected by the presence of oral contraceptive agents. There is one prominent exception; amprenavir levels, and probably fosamprenavir levels, are decreased, leading to a recommendation in the package insert that alternative methods of non-hormonal contraception should be used when taking fosamprenavir.[25] One note of caution with progesterone only contraception was recently reported at the Mexico City IAC meeting. Investigators of the Women's Interagency HIV Study (WIHS), a cohort of HIV infected and uninfected women, found that use of progestin-only contraception was associated with reduced HDL levels and increased insulin resistance.[26]

Several recently presented studies have addressed the issue of antiretroviral use in pregnancy.

Many physiologic changes occur during pregnancy; therefore, pharmacokinetic study results of several drugs have recently been reported. An interim analysis of pregnant women receiving atazanavir (300 mg daily) boosted with ritonavir (100 mg daily) together with zidovudine/lamivudine (300/150 mg twice daily) found that atazanavir exposure expressed as AUC and the C_{min} levels were decreased 40% and 21% respectively for women in the third trimester of pregnancy compared with historical controls.[27] Based on these findings, the investigators recommended increasing the atazanavir dose for HIV-infected women in the third trimester of pregnancy. At four weeks postpartum, the atazanavir drug levels were higher than historical controls, suggesting that pharmacokinetics revert to the non-pregnant state soon after delivery. Lower drug levels have also been demonstrated during the third trimester of pregnancy in women taking lopinavir/ritonavir (LPV/r),[28] and a recent study suggests that LPV/RTV (600/150 mg twice daily) be considered for use in the third trimester of pregnancy to assure appropriate LPV exposure.[29] However, when emtricitabine, a nucleoside reverse transcriptase inhibitor, pharmacokinetics were assessed in pregnancy, AUC decreased just 12%, precluding need for dose adjustment.[29]

Questions regarding birth defects in infants born to women on antiretroviral agents, however, remain.

The Antiretroviral Pregnancy Registry (APR) was established in 1989 to prospectively collect data on birth outcomes following antiretroviral exposure during pregnancy. Though this is an international registry, most of the reported data have, in fact, come from the U.S. The APR recently reported on birth defects rates from 987 women who took LPV/r during pregnancy, noting that this sample size was sufficient to detect a 2.4-fold increase in the risk of birth defects. The reported birth defect rate in this study of LPV/r exposed pregnancies was 2.4%, similar to the rate of 2.67% observed in the Metropolitan Atlanta Congenital Defects Program (MACDP) which was the control population.[30] The prevalence of birth defects following first trimester LPV/r exposure was 1.9%, again similar to the 2.09% first trimester early diagnosis rate of birth defects in the control population.[30] These results are the first adequately powered reported results for risk of birth defects in infants exposed to antiretroviral agents in utero. The Pregnancy Registry is an important available resource that assesses pregnancy outcomes. Health-care providers are asked to prospectively (before outcome of pregnancy is known) register women exposed to antiretroviral agents during pregnancy. Further information on the antiretroviral pregnancy registry is available at www.apregistry.com.

Antiretroviral Pregnancy Registry (APR) www.apregistry.com

Women in clinical trials: efficacy and side effects

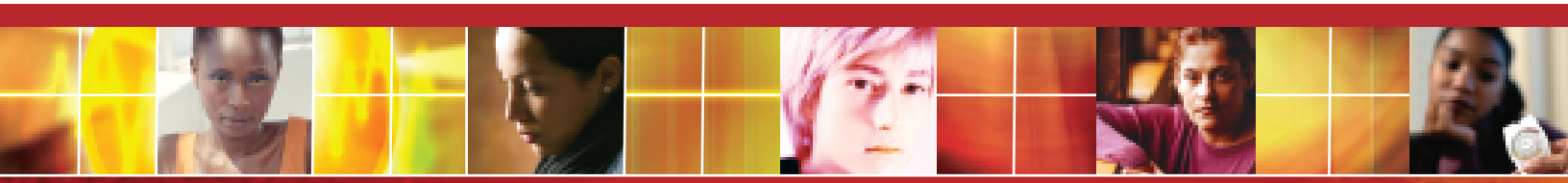
In recent years, women have participated in trials of new antiretroviral agents in sufficient numbers to permit assessment of outcomes based on sex, and such data from several trials were presented at the IAC meeting in Mexico City. The CASTLE study was a prospective, open-label randomized trial in treatment naïve persons comparing atazanavir/ritonavir (ATV/r) with lopinavir/ritonavir (LPV/r), both with tenofovir/ritonavir as the NRTI backbone. Overall in the Intention to Treat (ITT) analysis, the proportion of participants with HIV-1 RNA <50 copies/ml at week 48 (the primary endpoint) was 78% in the ATV/r arm and 76% in the LPV/r arm.[31] Women constituted 31% of the CASTLE study population and evaluation of virologic outcomes in men and women did not demonstrate any significant differences; 76% of women and 79% of men in the ATV/r arm compared with 73% of women and 78% of men in the LPV/r arms achieved HIV RNA <50 copies/ml.[32] $CD4^+$ count increases at 48 weeks were also similar; 199 cells/mm^3 and 205 cells/mm^3 in women and men respectively in the ATV/r arm compared with 221 cells/mm^3 and 219 cells/mm^3 in women and men respectively in the LPV/r arm. Side effects were generally similar among men and women with the exception that women were more likely to experience nausea in both arms of the study (7% and 3% in women and men respectively receiving ATV/r: 14% and 5% for women and men respectively receiving LPV/r), though women in the LPV/r arm were less likely than men to experience diarrhea (9% and 12% respectively).

To obtain continuing education credit, please complete the quiz, registration, and evaluation on the following pages, or go to: www.umdnj.edu/ccoe/aids

Trial results were also analyzed by sex in the ARTEMIS Trial, a prospective, multicenter, randomized trial comparing once daily darunavir/ritonavir (DRV/r) at 800 mg/100 mg with LPV/r each in combination with tenofovir/emtricitabine in antiretroviral-naïve patients. Overall, at 96 weeks, 79% of participants in the DRV/r arm had <50 copies/ml compared with 71% of participants in the LPV/r arm, thereby establishing superiority of DRV/r compared with LPV/r (*p* for superiority, <0.012).[19] Women constituted approximately 30% of ARTEMIS participants, and an analysis of 48-week outcomes by sex was recently presented. Eighty-four percent of both men and women in the DRV/r arm attained an HIV-1 RNA viral load <50 copies/ml at 48 weeks.[33] Women in the ARTEMIS trial were more likely to experience vomiting (11%) compared with men (4%). A sex-based analysis of the 96 week data has not been presented.

Finally, sex-specific outcomes data were also presented for the M05-730 trial, a multicenter, prospective, randomized trial in antiretroviral naïve patients comparing once daily LPV/r with twice daily LPV/r, each in combination with tenofovir/emtricitabine. The week 48 primary efficacy endpoint demonstrated that approximately 77% of participants in the once daily arm and 76% in the twice daily arm attained virologic suppression (HIV RNA <50 copies/ml).[34] Seventy-two percent of women and 78% of men achieved HIV-1 RNA <50 copies/ml at week 48, a difference that was not statistically significant.[35] Immunologic recovery was similar in men and women with the exception that for those individuals with baseline $CD4^+$ counts <50 cells/mm^3, mean $CD4^+$ increase in women was 237 cells/mm^3, while in men it was 167 cells/mm^3 (*p*=0.007). Adverse events were similar among men and women, however, grade 3 and grade 4 triglyceride abnormalities were less frequent in women than men (0.7% vs. 5.6% respectively; *p*=0.011).

(Continued on next page)



Women and HIV Treatment: Recently Reported Data

✦ **IN CONCLUSION,** a great deal of data has been presented at recent meetings addressing efficacy, safety and tolerability of antiretroviral agents, and recent DHHS guidelines updated on November 3, 2008 have reflected findings from some of the recently presented data.

✦ There are **EMERGING DATA** on pharmacokinetics of specific antiretroviral agents during pregnancy suggesting that dose modifications may be required for at least some protease inhibitors, and data on birth defect rates after in utero antiretroviral exposures are starting to emerge and, at least with lopinavir/ritonavir, are reassuring.

✦ **TO DATE,** sex based significant differences in virologic and immunologic responses to antiretroviral therapy have not been seen with the exception of better $CD4^+$ count responses in women with baseline $CD4^+$ counts <50 cells/mm^3 in the M05-730 trial.

✦ Finally, HIV care providers **MUST TAKE THE INITIATIVE WITH ALL PATIENTS** to discuss expectations and fears regarding antiretroviral therapy toxicity, assure clarity in regard to prevention of HIV transmission, and take the opportunity to discuss contraception and preconceptive care, particularly as relates to antiretroviral treatment and prevention of HIV transmission.

TO OBTAIN CONTINUING EDUCATION CREDIT:
Please complete the quiz, registration, and evaluation on the following pages, or go to: www.umdnj.edu/ccoe/aids

REFERENCES

1. Hecht FM, Busch MP, Rawal B, et al. Use of Laboratory tests and clinical symptoms for identification of Primary HIV-Infection. *AIDS.* 2002;16:1119-1129.
2. Hall HI, Song R, Rhodes P, Prejean J, Qian A, Lee L, Karon J, Bookmeyer R, Kaplan E, McKenna M, Janssen R. Estimation of HIV Incidence in the United States. *JAMA* 2008;300:520-529.
3. Centers for Disease Control and Prevention. HIV and AIDS in the United States: a picture of today's epidemic. http://www.cdc.gov/hiv/topics/surveillance/united_states.htm. Accessed September 19, 2008.
4. Centers for Disease Control and Prevention. HIV/AIDS Fact Sheet. HIV/AIDS among Women. Revised 2007.
5. 2000 Census at http://www.census.gov/popest/national/asrh/NC-EST2007/NC-EST2007-03.xls. Accessed November 14, 2008.
6. Gray A, Carlson R, Morgan M, Hawks D, Schulkin J. Gynecologists' knowledge and Practice regarding Human Immunodeficiency Virus Screening. *Obstet Gynecol.* 2007;110:1019-1026.
7. Hallfors DD, Iritani BJ, Miller WC, Bauer DF. Sexual and drug behavior patterns and HIV and STD racial disparities: the need for new directions. *Am J Public Health.* 2007;97:125-132.
8. Aberg J, Gallant J, Anderson J, et al. Primary Care Guidelines for the management of persons infected with Human Immunodeficiency Virus: Recommendations of the HIV Medicine Association of the Infectious Disease Society of America. *Clin Infect Dis.* 2004:39:609-629.
9. Sharma A, Feldman J, Golub E, Schmidt J, Silver S, Robinson E, Minkoff H. Live birth patterns among Human Immunodeficiency virus – Infected women before and after the availability of highly active antiretroviral therapy. *Am J Obstet Gynecol.* 2007:196:541.e1-541.e6.
10. Package Insert. Sustiva (Efavirenz). Princeton, NJ: Bristol-Myers Squibb. March 2008.
11. Arribas JR. Pozniak AL, Gallant JE, et al. Tenofovir disoproxil fumerate emtricitabine, and erfavirenz with Zidovudine/lamivudine and efavirenz in treatment naive patients: 144 Week Analysis. *J Acquir Immune Defic Syndr.* 2008 Jan 1;47(1):74-8.

REFERENCES

12. Haubrich R, Riddler S, DiRienzo G, et al. Metabolic outcomes of ACTG 5142: a prospective, randomized, phase III trial of NRTI-, PI, and NNRTI-sparing regimens for initial treatment of HIV-1 infection. Program and abstracts of the 14th Conference on Retroviruses and Opportunistic Infections; February 25-28, 2007; Los Angeles, California. Abstract 38.

13. Guidelines for the use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents, Department of Health and Human Services, November 3rd. 2008. http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf Accessed November 24, 2008.

14. Sax P, Tierney C, Collier AM, et al. ACTG 5202: Shorter time to virologic failure with ABC/3TC then tenofovir/FTC in Treatment-naïve Subjects with HIV RNA >100,000. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract THAB0303.

15. Smith KY, Fine D, Patel P, et al. Similarity in Efficacy and Safety of Abacavir/lamivudine (ABC/3TC) compared to tenofovir/emtricitabine (TDF/FTC) in Combination with Lopinavir/ritonavir (LPV/r) over 96 Weeks in the HEAT Study. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract LBPE1138.

16. D:A:D Study Group, Sabin CA,Worm SW,Weber R, et al. Use of Nucleoside reverse transcriptase inhibitors and risk of MI in HIV-infected patients enrolled in D:A:D Study: a multi-cohort Collaboration. *Lancet* 2008;371:1417-1426.

17. Strategies for Management of Antiretroviral Therapy/INSIGHT; D:A:D Study Groups. Use of nucleoside reverse Transcriptase Inhibitors and Risk of Myocardial Infarction in HIV. *AIDS* 2008; 22(14):F17-24.

18. Cutrell A, Hernandez Y, Yeo J, Brothers C, Yeo J, Burkle W, Spreen W. Is abacavir (ABC)-containing combination antiretroviral therapy (CART) associated with myocardial infarction (MI)? No association identified in Pooled Summary of 54 Clinical Trials. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract THAB0305.

19. Mills A, Nelson M, Jayaweera D, et al. ARTEMIS: efficacy and safety of darunavir/ritonavir (DRV/r) 800/100 mg once-daily vs. lopinavir/ritonavir (LPV/r) in treatment-naive, HIV-1-infected patients at 96 wks. In: Program and abstracts of the 48th Annual ICAAC/IDSA 46th Annual Meeting; October 25-28, 2008; Washington, D.C. Abstract H-1250c.

20. Averit Bridge D, Hodder S, Squires K, et al. Clinicians fail to routinely provide reproductive counseling to HIV-infected women in the United States. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0911.

21. Kasserra C, Adamczyk R, Li J, Sansone-Parsons A, O'Mara E. The Effect of Vicriviroc with or without ritonavir on oral contraceptive pharmacokinetics. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0043.

22. Sevinsky H, Eley T, He B, et al. Effect of Efavirenz on the Pharmacokinetics of Ethinyl Estradiol and Norgestimate in Healthy Female Subjects. 48th Annual ICAAC/46th Annual IDSA meeting.Washington DC. October 25-28, 2008. Poster A-958.

23. Package Insert. Kaletra (Lopinavir/Ritonavir) Tablet. North Chicago, Ill: Abbott Laboratories. December 2006.

24. Package Insert. Reyataz (atazanavir). Princeton, NJ: Bristol-Myers Squibb. September 2008.

25. Package Insert. Lexiva (fosamprenavir calcium). Research Triangle Park, NC. GlaxoSmithKline Pharmaceuticals. March 2008.

26. Womack J, Grey M, Williams, et al. Progestin-only contraception and metabolic outcome in women with and at risk for HIV. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract THPE0147.

27. Eley T, Vandeloise E, Child M, et al. Pharmacokinetics and clinical outcomes with atazanavir 300 mg QD/ritonavir 100 mg (ATV/r) QD + ZDV/3TC during the 3rd trimester of pregnancy in HIV+ women: interim results from BMS AI424182. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0121.

28. Stek AM, Mrochnck M, Capparell E, et al. Reduced lopinavir exposure during pregnancy. *AIDS* 2006;20:1931-1939.

29. Best B, Stek A, Hu C, et al.. FTC pharmacokinetics in pregnancy 2008 CROI,High-dose Lopinavir and Standard-dose Emtricitabine Pharmacokinetics during Pregnancy and Postpartum, 2008 CROI Abstract 629.

30. Roberts SS, Martinez M, Covington DL, Pasley MV, Woodward W. Lopinavir/ritonavir (LPV/r) in Pregnancy. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0120.

31. Molina JM, Andrade-Villanueva J, Echevarria J. Once-daily atazanavir/ritonavir versus twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine for management of antiretroviral-naïve HIV-1-infected patients: 48 week efficacy and safety results of the CASTLE study. *Lancet.* 2008;372:646-655.

32. Absalon J, Uy J, Rong Y, Mancini M, McGrath D. Gender-based differences in ARV-naïve patients treated with boosted protease inhibitors (PIs): results from the CASTLE study (AI424138). Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0062.

33. Andrade-Villanueva J, Hererra G, Chiliade P, Van Baelen B, Lefebvre E, Lavreys L. ARTEMIS: week 48 safety and efficacy of darunavir/r by gender, age, and race. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0064.

34. Gathe J, da Silva BA, Loutfy M, et al. Study M05-730 Primary Efficacy Results at Week 48: Phase 3 randomized, open-label study of lopinavir/ritonavir (LPV/r) tablets once daily (QD) versus twice daily (BID), co-administered with tenofovir DF (TDF) + emtricitabine (FTC) in antiretroviral-naive HIV-1 infected subjects. 15th Conference on Retroviruses and Opportunistic Infections (CROI); February 3-6, 2008. Boston, USA.

35. da Silva B, Cohen D, Gibbs, et al. Impact of Gender on Response to Lopinavir/ritonavir (LPV/r) Tablets dosed QD or BID Administered with Tenofovir Disoproxil Fumarate (TDF) and Emtricitabine (FTC) in Antiretroviral-naïve (ARV) Subjects: Results from Study M05-730. Program and Abstracts of the 17th International AIDS Conference; August 3-8, 2008; Mexico City. Abstract TUPE0069.

CONTINUING EDUCATION

Women and HIV Treatment: Recently Reported Data

Post-Test – Page 1 of 2

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. **Hallfors et al, in a study regarding HIV and sexually transmitted infection (STI) acquisition, with a population of 8,706 non-Latino blacks and whites 18-26 years of age, reported on racial and gender associations in a subgroup of individuals with low risk behaviors. What was the pattern they reported?**
   A. White men and women were more likely than their Black counterparts to acquire STIs and/or HIV.
   B. There was no significant difference between racial groups in rates of acquiring STIs and/or HIV.
   C. Black men were more likely than white men to acquire STIs and/or HIV, but there was no difference among women by racial group.
   D. Black men and women were more likely than their white counterparts to acquire STIs and/or HIV.

2. **In the DHHS guideline released November 3, 2008, which of the following nucleoside reverse transcriptase inhibitor agents were moved from preferred status to alternative status?**
   A. Tenofovir + emtricitabine
   B. Zidovudine + lamivudine
   C. Abacavir + lamivudine
   D. Tenofovir + abacavir

3. **In ACTG 5202, a trial comparing abacavir + lamivudine with tenofovir + emtricitabine, each in combination with efavirenz, why did an independent data safety monitoring board recommend early termination of the trial in the stratum of participants with baseline HIV RNA viral loads >100,000 copies/ml?**
   A. There was a higher rate of study defined virologic failure in the tenofovir + emtricitabine arm.
   B. There was a higher rate of myocardial infarction in the tenofovir + emtricitabine arm.
   C. The abacavir + lamivudine arm reached study defined virologic failure in a shorter time.
   D. There was a higher rate of myocardial infarction in the abacavir + lamivudine arm.

4. **While the pregnancy rate in HIV-uninfected women has increased 5% during the HAART era (1996-2008), what has happened to the pregnancy rate in HIV-infected women?**
   A. The rate decreased 150%.
   B. The rate increased 150%.
   C. The rate decreased 50%.
   D. The rate increased 50%.

5. **In a prospective cohort study, Hecht et al found which of the following strongly associated, by multivariate analysis, with presence of acute retroviral infection?**
   A. Fever
   B. Pharyngitis
   C. Cough
   D. Lymphadenopathy

6. **Ninety-six week data from the ARTEMIS trial, recently presented at 2008 ICAAC/IDSA, reported which of the following about Ritonavir boosted darunavir + tenofovir/emtricitabine?**
   A. It was superior to lopinavir/ritonavir + tenofovir/emtricitabine.
   B. It was non-inferior to lopinavir/ritonavir + tenofovir/emtricitabine.
   C. It was inferior to lopinavir/ritonavir + tenofovir/emtricitabine.
   D. It was inferior to lopinavir/ritonavir and abacavir/emtricitabine.

CE Activity Code: 110HC03- DE01

CONTINUING EDUCATION

Women and HIV Treatment: Recently Reported Data

Post-Test – Page 2 of 2

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).

---

7. The use of ritonavir in a woman who uses oral contraceptives which contain ethinyl estradiol will result in:

A. Increased blood levels of ethinyl estradiol.

B. Decreased blood levels of ethinyl estradiol.

C. No change in blood levels of ethinyl estradiol.

D. Increased blood levels of ritonavir.

8. The results from the "Women Living Positive Study," a recent anonymous phone interview of 700 HIV-infected women, found that what percentage of health care providers asked their HIV-infected patients about their current or future childbearing plans?

A. Less than 10% of the participants were asked about childbearing plans.

B. Almost half of those surveyed, 48%, were never asked about childbearing plans.

C. Roughly 90% were asked about childbearing plans.

D. This survey did not address provider communication with patients.

9. The Antiretroviral Pregnancy Registry recently reported on birth defects rates from 987 women who took LPV/r during pregnancy, compared with the rate of birth defects (2.67%) observed in a control population, the Metropolitan Atlanta Congenital Defects Program (MACDP). Which of the following is true?

A. Similar rates of birth defects were reported for infants exposed in utero to LPV/r (2.4%) vs. the control population.

B. The prevalence of birth defects following first trimester LPV/r exposure was 1.9%, similar to the 2.09% first trimester early diagnosis rate of birth defects in the control population.

C. These results are the first adequately powered reported results for risk of birth defects in infants exposed to antiretroviral agents.

D. All of the above.

10. Several recent trials, CASTLE, ARTEMIS, and M05-730, have assessed virologic outcome by sex. Which of the following statements is (are) true?

A. Women consistently demonstrated significantly better virologic and immunologic outcomes than men.

B. There were no significant differences among men and women with respect to virologic and immunologic outcomes.

C. There were no significant differences in the immunologic outcomes in these studies, however, significantly better virologic outcomes were observed in men in the ARTEMIS trial.

D. There were no significant differences in the virologic outcomes in these studies, however, women with baseline $CD4^+$ counts <50 cells/mm^3 demonstrated significantly greater increases in $CD4^+$ cells than did men with baseline $CD4^+$ counts <50 cells/ mm^3 in the M05-730 trial.

CE Activity Code: 110HC03- DE01

CONTINUING EDUCATION

Women and HIV Treatment: Recently Reported Data

Registration Form

CCOE
Center for Continuing & Outreach Education

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)™* 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.

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.umdnj.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 *Circle the best answer for each question.*	**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

– PLEASE PRINT –

First Name _____ M.I. _____ Last Name _____ Degree _____

Daytime Phone # _____ Evening Phone # _____

Fax # _____ E-mail _____

Preferred Mailing Address: ☐ Home ☐ Business

Address _____

City _____ State _____ Zip Code _____

Affiliation/Specialty _____

Indicate the type of continuing education credit you wish to obtain as a result of your participation in this activity.

☐ **Nurses:** Nursing contact hours (ANCC): Hours awarded: 1.25

☐ **Physicians**: *AMA PRA Category 1 Credit(s)™* Credit Letter: Credits Claimed: _____

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

One credit for each hour of participation (ANCC, AMA); not to exceed 1.0 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.

Signature _____ Date _____

Release date: January 2009 • **Expiration date:** Credit for this activity will be provided through June 30, 2010.
Nursing Credit for this activity will be provided through June 30, 2010.

UMDNJ-Center for Continuing & Outreach Education
PO Box 1709, Newark, New Jersey 07101-1709
Phone: 973-972-4267 or 1-800-227-4852 • Fax: 973-972-7128

CE Activity Code: 11HC03- DE01
This form may be photocopied.

CE CONTINUING EDUCATION

Women and HIV Treatment: Recently Reported Data

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.

CCOE Center for Continuing & Outreach Education

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

PROGRAM OBJECTIVES:		**Strongly Agree**				**Strongly Disagree**
Having completed this activity, are you better able to:						
Objective 1:	Summarize the epidemiology of HIV infection in US women.	5	4	3	2	1
Objective 2:	Identify antiretroviral drug interactions with oral contraceptives and changes in pharmacokinetics that may occur with antiretroviral dosing in pregnancy	5	4	3	2	1
Objective 3:	Describe recent antiretroviral clinical trial results, including comparison of outcomes among men and women.	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:

CE Activity Code: 11HC03- DE01

This form may be photocopied.

CONTINUING EDUCATION

HIV Testing Update

Release Date: January 2009 • Expiration Date: June 30, 2010 • Course Code: 11HC02-DE01
Nursing Credit for this activity will be provided through June 30, 2010.

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 adults and adolescents.

Statement of Need

HIV testing recommendations have changed significantly over the years, since HIV testing first became available in 1985, with the principal goal of protecting the blood supply. Special HIV test sites were established so people would not use blood banks to learn their HIV status. Since then, both HIV testing and treatment have become effective. The CDC currently recommends that all healthcare providers integrate HIV counseling and testing into routine practice.

HIV treatment success depends, in part, on timely diagnosis of infection. The CDC reports that during 2005, 38% of people diagnosed with AIDS had their initial positive HIV test less than one year earlier.[1] The state of New Jersey has legislated "Opt-Out" HIV screening for all pregnant women, in the first and third trimesters of prenatal care, and testing of newborns whose mothers do not have an HIV test record.[2]

Clinicians and health administrators need current information about the most effective and efficient means to diagnose and confirm HIV infection, to implement expanded HIV testing programs in medical care. Increased testing and earlier diagnosis of HIV infection will reduce treatment delays for persons with HIV infection and help them to live longer and healthier lives.

[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): 1-17.
[2] Paul, S.M. and Dimasi, L.G. New Jersey's New Legislation for HIV Testing of Pregnant Women and Newborns. *New Jersey AIDSLine* June 2008:1, 36.

Learning Objectives

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

1. Describe the most recent Centers for Disease Control and Prevention recommendations for HIV testing.
2. Explain the indications for rapid HIV testing of women in labor and some newborns.
3. Describe the licensing requirements for rapid HIV testing.

Activity Director(s)/CME Academic Advisor(s)

• Patricia Kloser, MD, MPH, UMDNJ-NJ Medical School

Planning Committee

• Sindy Paul, MD, MPH, FACPM, New Jersey Dept. of Health and Senior Services
• Debbie Y. Mohammed, MS, MPH, APRN-BC, UMDNJ-University Hospital
• Linda Berezny, RN, BA
• Kimi Nakata, MSW, MPH, UMDNJ-CCOE

Faculty

Sindy M. Paul, MD, MPH, FACPM, is the Medical Director of the NJ Dept. of Health and Senior Services, Division of HIV/AIDS Services; Assistant Clinical Professor at the UMDNJ-School of Public Health and past President, New Jersey Board of Medical Examiners.

Eugene Martin, PhD, is Professor of Pathology and Laboratory Medicine at UMDNJ-Robert Wood Johnson Medical School and Administrative Director, University Diagnostic Laboratories (UDL) and UDL Subdirector, Point of Care Testing.

Method of Instruction

Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the self-assessment test which consists of a series of multiple-choice questions. Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a credit letter and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials; or may complete the activity on the internet at www.umdnj.edu/ccoe. Estimated time to complete this activity as designed is 1.25 hours.

Accreditation

Physicians: UMDNJ-Center for Continuing and Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. UMDNJ-Center for Continuing and Outreach Education designates this educational activity for a maximum of 1.25 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nurses: The University of Medicine and Dentistry of New Jersey-Continuing Education and Outreach Education is an approved provider of continuing nursing education by the New Jersey State Nurses Association, Provider Number P173-10/06-09. New Jersey State Nurses Association is accredited by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is awarded 1.25 contact hours.

UMDNJ-Center for Continuing and Outreach Education is an approved provider of continuing education by the California Board of Registered Nursing, Provider Number CEP 13780 for a maximum of 1.25 contact hours for this activity.

Review: This activity was peer reviewed for relevance, accuracy of content, and balance of presentation by Patricia Kloser, MD, MPH; Debbie Y. Mohammed, MS, MPH, APRN-BC, and Brenda Christian, MEd, PA-C; and pilot tested for relevance and time required for participation by Kinshasa Morton, MD; Bonnie Abedini, BSN, RN; Mary C. Krug, RN, MSN, APN-C; and Kara Winslow, BSN, RN.

Faculty Disclosure Declarations

Debbie Mohammed has disclosed the following: she is on the speaker's bureaus of BMS and Gilead.

Conflicts of interest were resolved by review by Activity Director Patricia Kloser, MD, MPH.

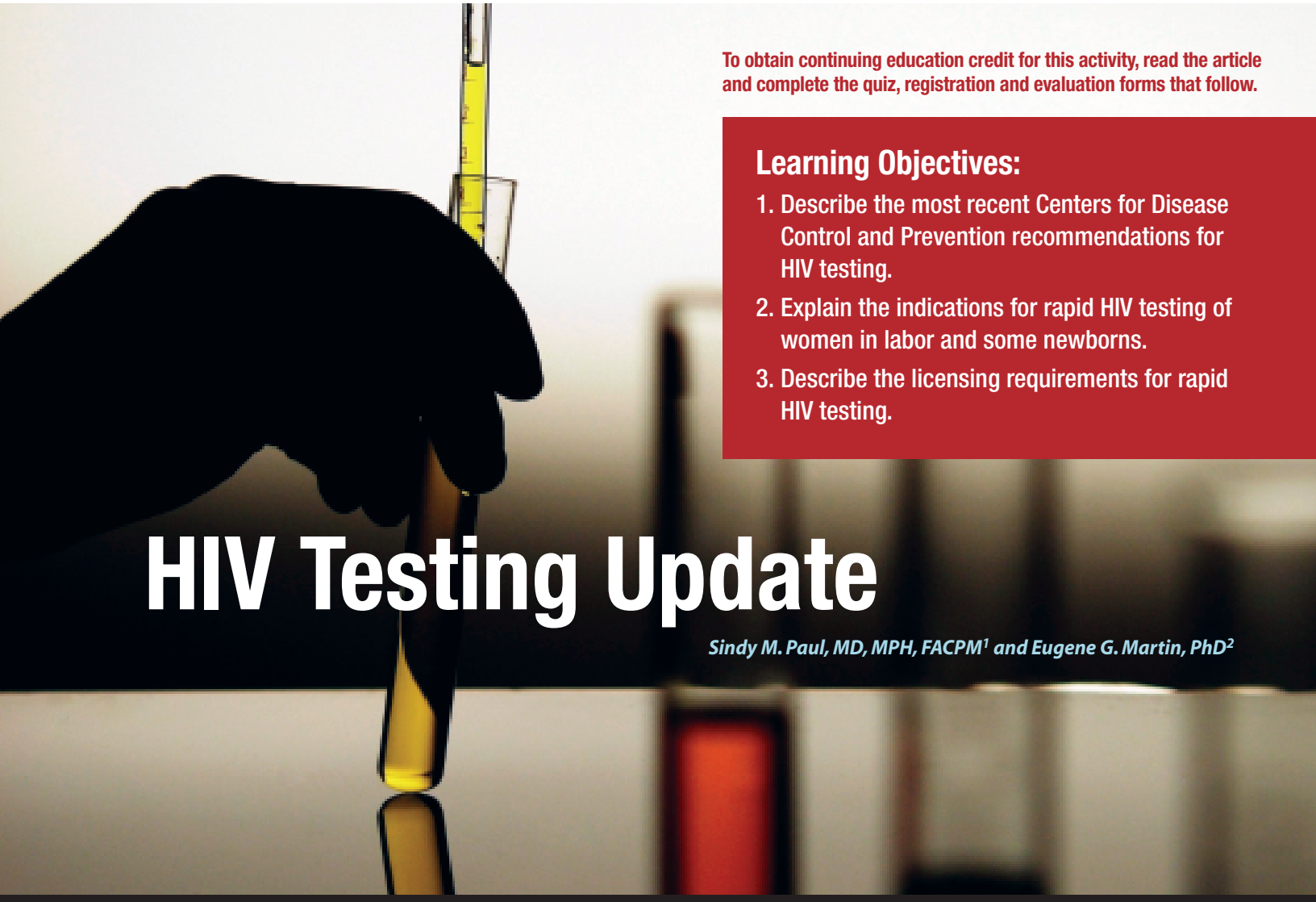
The following have no financial relationships to disclose: Activity Director Patricia Kloser, MD, MPH; Planning committee members Sindy M. Paul, MD, MPH, FACPM; Linda Berezny, RN, BA; and Kimi Nakata, MSW, MPH (editor); content reviewer Brenda Christian, MEd, PA-C; and field testers: Kinshasa Morton, MD; Bonnie Abedini, MSN, RN; Mary C. Krug, RN, MSN, APN-C; and Kara Winslow, BSN, RN.

Off-Label Usage Disclosure

This activity does not contain information of commercial products/devices that are unlabeled for use or investigational uses of products not yet approved. Vicriviroc is currently in Phase II/III clinical trials. Darunavir is in FDA Pregnancy Category B, and lopinavir/r is in FDA Pregnancy Category C; each should be used only if the potential benefit justifies the potential risk.

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.



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

Learning Objectives:

1. Describe the most recent Centers for Disease Control and Prevention recommendations for HIV testing.
2. Explain the indications for rapid HIV testing of women in labor and some newborns.
3. Describe the licensing requirements for rapid HIV testing.

HIV Testing Update

Sindy M. Paul, MD, MPH, FACPM[1] and Eugene G. Martin, PhD[2]

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) estimates that more than one million people in the United States are infected with HIV[1]. Of these, 24 to 27 percent do not even know that they are infected.[2] The CDC also estimates that 56,300 people in the United States became infected with HIV in 2006.[3] Unfortunately, HIV testing rates among adults have remained virtually flat over the last five year while surveys suggest that nearly 40% of adults believe that they had never been tested for HIV.[4]

(Continued on next page)

Release Date: January 2009 • Expiration Date: June 30, 2010 • Course Code: 11HC02-DE01 • Nursing Credit for this activity will be provided through June 30, 2010.

[1] *New Jersey Department of Health & Senior Services, Trenton, NJ*
[2] *University of Medicine & Dentistry of New Jersey, Robert Wood Johnson Medical School, Dept. of Pathology & Laboratory Medicine, New Brunswick, NJ*

Sponsored by the University of Medicine & Dentistry of New Jersey (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.

Although the success of treatment depends, in part, on timely diagnosis of an HIV infection; HIV treatment with the combination of highly active antiretroviral therapy (HAART), and the improved management of opportunistic infections has markedly improved HIV survival rates.[5] According to CDC data in 2005, 38% of people with AIDS had their initial positive HIV test less than one year before their AIDS diagnosis.[6] In the HAART era, it is more important than ever to diagnose HIV disease earlier, so effective treatment can be provided.

HIV testing began in the mid 1980's with the development of a first generation enzyme immunoassay (EIA) for HIV[1]. This was followed by FDA approval for the use of a supplemental Western blot (WB) confirmatory test in 1987 which was designed to improve the specificity of the diagnostic process.

Early in the AIDS pandemic, laboratory tests were developed with a primary purpose of protecting the nation's blood supply.[7,8] At that time the risk of HIV infection through transfusion was approximately 1 in 100. Estimates in 2004 placed the risk at approximately 1 in 1.9 million.[9]

Early enzyme-based immunoassays were relatively insensitive, and not very specific. A significant contributor to false positive results, seen with first generation HIV assays, was the necessity of propagating the HIV virus in tissue culture since the virus assembles and buds from the host cell membranes. The use of tissue culturing techniques and viral lysates in the manufacturing process led to the co-purification of host cellular proteins. As a result, assays occasionally responded to antibodies against the host cell antigens rather than antigens related to an HIV infection itself.[10]

Over the years, diagnostic manufacturers worked to maximize test sensitivity and improve the specificity. To minimize false positive results, the U.S. Food and Drug Administration (FDA) mandated that every test would need to be confirmed by an independent procedure (an immunofluorescence-based assay (IFA) or a Western blot (WB)) before an HIV result could be declared final and reported to a patient. In 1989, the CDC and the Association of Public Health Laboratories (APHL) recommended the combination of an EIA and a WB as the "gold standard" for the diagnosis of HIV infection.[11]

In the 1990's, a better understanding of the serologic evolution of an HIV infection led diagnostic companies to develop assays better tailored to the immunologic response and the serologic pattern of an HIV infection. At present, there are sensitive and specific antibody tests, tests that detect antigens present during the early stages of an HIV-1 infection, assays that respond to both IgG and IgM antibodies, as well as assays that target the molecular biology of the HIV infection itself.

HIV screening depends on detecting the presence of HIV antibodies. Determining the stage of an HIV infection is more complicated and depends on the pattern of antigens and antibodies. A known serologic window exists between the time that an HIV infection begins, and the time when diagnostic tests are able to detect the antigen or antibody responses to that infection.[12] Because of the limited duration of the antigenic response, HIV screening is usually conducted by testing for the presence of HIV antibodies which arrive a little later, but persist until an individual is severely immunodeficient. When there is clinical indication suggesting a recent HIV exposure, additional diagnostic testing may include tests for HIV p24 antigen, as well as nucleic amplification to look for molecular evidence of HIV-1 RNA.

During the past five years, the FDA has approved six rapid HIV tests (four of which are Clinical Laboratory Improvement Amendments of 1988 (CLIA)-waived for point-of-care-testing (POCT); two third-generation EIA tests that can detect HIV-1, HIV-2, and HIV-Group O; a qualitative diagnostic RNA assay (Aptima, Gen-Probe); and the new quantitative viral load assays. Additional HIV tests may soon be available in the United States, including a fourth generation EIA that recognizes elements of both the antigen and antibody response to an HIV infection and markedly reduces the serologic window.[9]

For more than 20 years, traditional antibody testing processes have relied upon approaches designed to maximize sensitivity without sacrificing specificity. This is achieved by a multi-step algorithm that is consistent with the operation of a traditional clinical laboratory. Unfortunately the traditional laboratory algorithm often took days to weeks to complete. The advent of point-of-care testing (POCT), combined with the realization of the important barrier that results from "test anxiety" and the significant numbers of individuals who consequently fail to return to receive a confirmatory result, have propelled the recent awareness that ***HIV screening and confirmation need to be accomplished simultaneously if public health authorities are to maximize the effectiveness of the HIV screening programs.***

CONVENTIONAL LABORATORY TESTING ALGORITHMS RELY UPON:
- **An initial, single EIA screening test,**
- **Followup replicate EIA tests,**
- **And additional, highly complex confirmatory procedures.**

In conventional HIV testing, where clients must return several days later to learn their results, nearly 25% of the clients fail to return for the second meeting. This makes it clear that the conventional testing algorithm is neither cost-effective nor sufficient HIV screening.

HIV Testing Recommendations

HIV testing recommendations have changed significantly over the years. As noted earlier, when HIV testing first became available in 1985, the principal goal was protecting the blood supply. Ambulatory HIV testing sites were established so people would not use blood banks for HIV testing to learn their HIV status. The value of HIV testing was controversial in 1985. No consensus existed on whether a positive test predicted transmission to sex partners or from mother-to-child, no effective treatment existed, and counseling was designed in part to ensure that the people who were tested were aware that the meaning of positive test results was uncertain.[8,13] Through the years this uncertainty has been clarified, effective treatment became available, and the role of antiretroviral agents to reduce the risk of occupational and perinatal HIV transmission has been defined. The CDC currently recommends that all healthcare providers integrate HIV counseling and testing into routine practice.[14]

In September 2006, the CDC published recommendations for HIV testing of adults, adolescents, and pregnant women. In these recommendations, the CDC advocates routine, voluntary HIV screening as a normal part of medical practice, similar to screening for other treatable conditions. Screening is viewed as a basic public health tool used to identify communicable diseases, so preventive measures can be taken to reduce the risk of transmission and treatment can be offered before symptoms develop.[1] The World Health Organization (WHO) has also established screening criteria. The HIV screening tests are reliable, inexpensive, and non-invasive. If HAART is initiated early, before the person is symptomatic, the patient has years of life to gain. The costs of HIV screening are reasonable in relation to the anticipated benefits of a healthier life, longer life, and better quality of life when treatment can start before the immune system is compromised.[8,15] Studies have shown that HIV screening, in populations with a prevalence of undiagnosed HIV infection >0.1%, is as cost-effective as other established screening programs for chronic diseases (e.g., hypertension, colon cancer, and breast cancer).[8,16,17]

Population-based HIV screening of pregnant women has proven substantially more effective than risk-based testing for detecting unsuspected maternal HIV infection, and preventing perinatal transmission.[1] Perinatal HIV transmission in the United States decreased from 945 cases in 1992 to 48 cases in 2004. This 95% reduction is associated with CDC recommendations for HIV screening of pregnant women and for obstetrical care of HIV-positive women, and use of antiretroviral agents to reduce the risk of vertical HIV transmission.[8,18]

SEPTEMBER 2006 CDC RECOMMENDATIONS FOR HIV SCREENING FOR ADULTS & ADOLESCENTS

"Initial" HIV screening recommendations

- In all healthcare settings, screening for HIV infection should be performed routinely for all patients aged 13-64 years. Healthcare providers should initiate screening, unless prevalence of undiagnosed HIV infection in their patients has been documented to be <0.1%. In the absence of existing data for HIV prevalence, healthcare providers should initiate voluntary HIV screening until they establish that the diagnostic yield is <1 per 1,000 patients screened, at which point such screening is no longer warranted.[1]
- All patients initiating treatment for TB should be screened routinely for HIV infection.[1]
- All patients seeking treatment for STDs, including all patients attending STD clinics, should be screened routinely for HIV during each visit for a new complaint, regardless of whether the patient is known or suspected to have specific behavior risks for HIV infection.[1]

"Repeat" HIV screening recommendations

- All people likely to be at high risk for HIV should have repeat screenings, at least annually. This includes injection-drug users and their sex partners, persons who exchange sex for money or drugs, sex partners of HIV-infected persons, MSM, or heterosexual persons who themselves, or whose sex partners have had more than one sex partner since their most recent HIV test.[1]
- Patients and their prospective sex partners should be encouraged to be tested before initiating a new sexual relationship.[1]
- Repeat screening of people not likely to be at high risk for HIV should be performed on the basis of clinical judgment.[1]
- Unless recent HIV test results are immediately available, any person whose blood or body fluid is the source of an occupational exposure for a healthcare provider should be informed of the incident, and tested for HIV infection at the time the exposure occurs.[1] However, you need to check with the state and local laws and regulations regarding the need for consent and confidentiality of test results.

Consent and provision of pre-test information are also addressed in the September 2006 CDC recommendations. Screening should be voluntary and done only with the patient's knowledge and understanding that HIV testing is planned. Patients should be informed orally or in writing that HIV testing will be performed unless they decline (opt-out screening).[1] However, you need to check with the state and local laws and regulations to make sure that opt-out testing can be done in your jurisdiction.

The CDC recommends that oral or written information should include an explanation of the HIV infection and the meanings of positive and negative test results. Importantly, the patient should be offered an opportunity to ask questions and to decline testing. The information should be made available in the languages commonly encountered within the catchment area. The competence of interpreters and bilingual staff to provide language assistance to patients with limited English proficiency must be ensured. With such notification, consent for HIV screening should be incorporated into the patient's general informed consent for medical care on the same basis as are other screening or diagnostic tests; a separate consent form for HIV testing is not recommended.[1] Clinicians should confirm that state and local laws and regulations allow inclusion of HIV testing in the general consent. If a patient declines an HIV test, this decision should be documented in the medical record.

DIAGNOSTIC HIV TESTING
is not the same as HIV screening.

Diagnostic testing is performed based on a clinical suspicion of HIV infection.

The September 2006 CDC recommendations for diagnostic HIV testing of adults and adolescents are summarized below.

- All patients with signs or symptoms consistent with HIV infection should be tested for HIV.[1]
- All patients with an opportunistic illness characteristic of AIDS should be tested for HIV.[1]
- Clinicians should maintain a high level of suspicion for acute HIV infection in all patients who have a compatible clinical syndrome and who report recent high-risk behavior. When acute retroviral syndrome is a possibility, a plasma RNA test should be used in conjunction with an HIV antibody test to diagnose acute HIV infection.[1]
- Patients or those responsible for the patient's care should be notified orally that testing is planned, advised of the indication for testing, and the implications of positive and negative test results, and offered an opportunity to ask questions and to decline testing. With such notification, the patient's general consent for medical care is considered sufficient for diagnostic HIV testing.[1] Clinicians should confirm that state and local laws and regulations allow inclusion of HIV testing in the general consent.

Recommendations for Pregnant Women and Their Infants

Knowledge of the HIV status is the key to reducing the risk of vertical HIV transmission. All women should receive HIV screening consistent with the recommendations for adults and adolescents described above.[1] To maximize the opportunity for women to know their HIV status prior to pregnancy, HIV screening should also be a routine component of the preconception care.[19] Conducting HIV screening as early as possible in pregnancy allows HIV-infected pregnant women and their infants to benefit from appropriate and timely interventions, such as antiretroviral agents, cesarean delivery (if the maternal viral load is greater than 1,000), and avoidance of breast feeding.[20]

The September 2006 CDC recommendations for universal opt-out HIV screening of pregnant women and their infants are summarized below.

- All pregnant women in the United States should be screened for HIV infection. Typically, as part of standard pre-natal care, an expectant mother will be notified that HIV screening is recommended for all pregnant patients and that she will receive an HIV test as part of a routine panel of prenatal tests, unless she declines (opt-out screening). This HIV screening should be performed as early in the pregnancy as possible. Women who decline the test early in prenatal care, should be encouraged to be tested at a subsequent visit.[1] Where allowed by state and local laws and regulations, the CDC recommends opt-out HIV testing.[1]
- A second HIV test during the third trimester, preferably <36 weeks of gestation, has been shown to be cost-effective even in areas of low HIV prevalence, and may be considered for all pregnant women.

A second HIV test during the third trimester is recommended for women who meet one or more of the following criteria:

- Women who receive healthcare in jurisdictions with elevated incidence of HIV or AIDS among women aged 15-45 years. In 2004, these jurisdictions included Alabama, Connecticut, Delaware, the District of Columbia, Florida, Georgia, Illinois, Louisiana, Maryland, Massachusetts, Mississippi, Nevada, New Jersey, New York, North Carolina, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, and Virginia.
- Women who receive healthcare in facilities in which prenatal screening identifies at least one HIV-infected pregnant woman per 1,000 women screened.
- Women who are known to be at high risk for acquiring HIV (e.g., injection-drug users and their sex partners, women who exchange sex for money or drugs, women who are sex partners of HIV-infected persons, and women who have had a new or more than one sex partner during this pregnancy).

Women who have signs or symptoms consistent with acute HIV infection

When acute retroviral syndrome is a possibility, a plasma RNA test should be used in conjunction with an HIV antibody test to diagnose acute HIV infection.[1]

- HIV testing must be voluntary and free from coercion. No woman should be tested without her knowledge.[1]
- Pregnant women should receive oral or written information that includes an explanation of HIV infection, a description of interventions that can reduce HIV transmission from mother to infant, and the meanings of positive and negative test results, and should be offered an opportunity to ask questions, and to decline testing.[1]
- No additional process or written documentation of informed consent beyond what is required for other routine prenatal tests should be required for HIV testing.[1] Clinicians should confirm that state and local laws and regulations allow inclusion of HIV testing in the general consent.[1]
- If a patient declines an HIV test, this decision should be documented in the medical record. The reasons for declining HIV testing need to be discussed and addressed. Women who decline an HIV test because they have had a previous negative test result should be informed of the importance of re-testing during each pregnancy. Logistical reasons for not testing, such as scheduling should be resolved. Some women who initially decline an HIV test may accept testing at a later date, especially if their concerns are discussed. Some women will continue to decline testing, and their decisions should be respected and documented in the medical record.[1]

SOME WOMEN PRESENT IN LABOR WITHOUT A DOCUMENTED HIV TEST.

Rapid HIV testing is recommended for women in labor without a HIV test. Postpartum/newborn screening is also advised in specific circumstances. The September 2006 CDC guidelines are summarized below.

- Any woman with an undocumented HIV status at the time of labor should be screened with a rapid HIV test unless she declines (opt-out screening).[1,18] Clinicians should confirm that state and local laws and regulations allow inclusion of HIV testing in the general consent[1]
- The reasons for declining a rapid HIV test should be explored and addressed as described above.[1]
- Immediate initiation of appropriate antiretroviral prophylaxis should be recommended to women on the basis of a reactive rapid HIV test result without waiting for the result of a confirmatory test.[1,21] The most recent Public Health Service Task Force recommendations are available at http://aidsinfo.nih.gov.[16]
- When a woman's HIV status is still unknown at the time of delivery, she should be screened immediately postpartum with a rapid HIV test unless she declines (opt-out screening).[1] However, you need to check with the state and local laws and regulations to make sure that opt-out HIV testing can be done in your jurisdiction.
- When the mother's HIV status is unknown postpartum, rapid HIV testing of the newborn is recommended as soon as possible after birth, so antiretroviral prophylaxis can be offered to HIV-exposed infants. Women should be informed that identifying HIV antibodies in the newborn indicates that the mother is infected. Some states require newborn testing, so you need to be aware of the laws and regulations regarding newborn screening in your jurisdiction.[1]
- For infants whose HIV exposure status is unknown and who are in foster care, the person legally authorized to provide consent should be informed that rapid HIV testing is recommended for infants whose biologic mothers have not been tested.[1]
- The benefits of neonatal antiretroviral prophylaxis are best realized when it is initiated <12 hours after birth.[1]

Some states have developed laws and/or regulations related to HIV testing of pregnant women.

New Jersey Assembly P.L. 2007, c.218. was signed into law on December 26, 2007 by Acting Governor Richard J. Codey, and went into effect in July 2008. This legislation requires New Jersey healthcare providers to test pregnant women for HIV as part of the routine prenatal care as early in the pregnancy as possible, and again during the third trimester unless the woman refuses testing. Voluntary, opt-out, universal rapid HIV testing is required for women who present in labor with unknown HIV status or who have not been tested in the third trimester. It also requires newborn rapid HIV testing if the HIV status of the mother of the newborn is unknown. However, the newborn will not be tested if the parents object to the test as being in conflict with their religious tenets and practices, and they provide a written statement of this objection for inclusion in the newborn's medical record. The legislation follows the most recent CDC recommendations for HIV testing of pregnant women.[1,22]

(Continued on next page)

Rapid HIV Testing

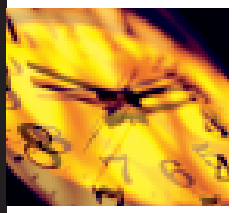
Rapid diagnostic HIV tests and the availability of CLIA-waived rapid HIV testing has clinical implications for:

1. Assisting in the diagnosis and counseling of persons with HIV disease;
2. Reducing the risk of occupational and non-occupational HIV transmission;
3. Reducing the risk of occupational HIV transmission; and
4. Reducing the risk of vertical HIV transmission, particularly for women in labor with unknown HIV status.[8,23-25]

The decision for post exposure antiretroviral agent prophylaxis can be based on rapid HIV test results. The use of rapid HIV tests in clinical care settings can substantially improve the delivery of HIV counseling and testing (CT) services, because patients can receive their results the same day.

Patients who have HIV counseling and testing and do not return to receive their test results and post-test counseling have been a major public health concern in the United States. The CDC reported that of 2.5 million people tested in 1995, 25% of those testing positive and 33% of those testing negative did not receive their test results. The CDC calculated that a total of 697,495 more people nationwide would have learned their HIV status if rapid HIV testing was used.[26]

Rapid point-of-care diagnostic HIV tests offer the advantage that people do not need to return to obtain their test results. More people know their HIV status, and if infected, can be referred for treatment, prevention programs, and social services much more rapidly. People who know they are infected with HIV are more likely to practice risk-reduction, especially, if a brief behavioral intervention is conducted at the patient visit.[27]



There have been many changes in HIV testing since the development of the original EIA and WB. At the forefront of recent advances are rapid diagnostic HIV tests and CLIA-waived rapid HIV tests, whichallow integration of HIV screening into daily clinical practice.

Interpretation of Rapid HIV Tests

Interpretation of rapid HIV tests is the same as other, conventional HIV screening tests. A negative result from a single test is interpreted as being negative. However, if a person is at risk of having been exposed to HIV within three months of the test, a repeat test at a later time is recommended. A positive (or reactive) result is considered to be a preliminary positive test result. This must be confirmed using a Western blot, an immunofluoresence assay (IFA), or Aptima. This confirmatory testing should be done as soon as possible. If the rapid HIV test is a preliminary positive and the confirmatory test is negative (discrepant results) both the rapid HIV test and the confirmatory test should be repeated. A consultation with an infectious disease specialist is recommended. If the rapid HIV test does not provide a valid test result, most likely the test kit did not work properly and the rapid HIV test should be repeated.[28]

Counseling Patients with a Negative Rapid HIV Test

Patients whose rapid HIV test result is negative can be told that they are not infected, unless they have had a recent (within 3 months) known or possible exposure to HIV. Retesting should be recommended for these patients because sufficient time needs to elapse in order for development of the antibodies that are detected by the test.[29]

Counseling Patients with a Preliminary Positive Rapid HIV Test

Confirmatory testing is always required to confirm a reactive rapid HIV test result. The challenge is providing reactive (preliminary positive) results to patients without the benefit of a same-day confirmatory test. For all patients with a reactive rapid HIV test result, however, it is essential to:

- Explain that this is a preliminary test result that needs to be confirmed.
- Emphasize the importance of confirmatory testing and schedule a return visit for the confirmatory test results.

Underscore the importance of taking precautions to avoid the possibility of transmitting infection to others while awaiting results of confirmatory testing.[29]

Rapid HIV Testing Compared to Traditional EIA Testing

Point-of-care, rapid HIV testing is likely to become more available as physician offices begin to implement the CDC recommendations to include HIV testing as a part of routine healthcare. Rapid HIV testing will play an important role in providing HIV screening in the physician's office. It will play a smaller role in the diagnostic assessment of individuals who have very recently engaged in high-risk activities and in individuals who have already elicited clinical suspicion of a possible acute HIV exposure.[8]

HIV prevention and screening programs have found that the availability of rapid HIV testing is associated with increased client demand for testing in public health settings, increased program follow-up with clients, and subtle changes in the characteristics of clients who agree to be tested.[30]

HIV testing by a highly sensitive third generation EIA, followed by a more specific WB or immunofluorescence assay, is comparable to rapid HIV screening by means of lateral flow immunochromatographic devices, and follow-up testing by WB. Currently, the sensitivity and specificity of rapid HIV testing exceed 99.6% and 99.8%, respectively. Compared to first generation HIV EIAs, still in use in some public health laboratories, current rapid HIV tests are more sensitive and specific. Examples have been reported of HIV RNA-containing specimens that are non-reactive by third generation EIA, and yet repeatedly reactive using the Uni-Gold Recombigen HIV-specific antibody rapid test.[31]

Laboratory Testing for HIV 1/2 – Enzyme Immunoassays

Since the very first EIAs were developed to permit HIV detection nearly 20 years ago, the quality and performance of these tests has steadily improved, first by the use of synthetic peptides and recombinant antigens (second generation assay), and later by the use of a sandwich EIA technology (third generation).[32,33]

Internationally, fourth generation assays have been introduced which allow simultaneous detection of both HIV antigen, as well as, the HIV antibody, and thus effectively shrink the serologic window from infection to detection. Unfortunately, early fourth generation assays have been troubled by relatively poor antigen detection sensitivity and a somewhat higher rate of false-positive results than third-generation EIA.[34,35] At present, no fourth generation assay is approved for use in the United States.

Early HIV EIAs were designed to maximize sensitivity. Based upon whole virus or virus lysate technology, results were occasionally associated with non-specific reactions caused by antibodies responding to human cell proteins present in the antigen preparations. Sometimes false positive specimens were associated with autoimmune diseases, multiple pregnancies, anti-HLA, EBV infections, or hypergammaglobulinemia. The development of second-generation assays largely resolved those issues by the use of proteins which corresponded to viral proteins derived by bacterial recombinant DNA technology.[36]

Present generation HIV 1/2 EIAs have outstanding sensitivity and specificity. Virtually all assays currently in use have sensitivity in excess of 98.5% and specificity in excess of 99.1%.[37] Nonetheless, concerns remain over the risk of false negative results in infected individuals. Potential causes of negative results include the so-called "diagnostic window" which occurs prior to seroconversion, HIV genetic variability, and atypical seroconversions, delayed or absent immune response in the very early or advanced stages of infection, respectively.[38]

Early detection is important for "at risk" clinical diagnosis, prevention of transmission, and for ensuring the safety of the blood supply.[39] Several HIV antigen-antibody (Ag/Ab) combination assays that simultaneously detect HIV-1 p24 antigen, as well as, antibodies to HIV-1 group M, group O, and HIV-2 are also available, but only outside the United States. These combination assays are able to reduce the seroconversion window by 3-5 days relative to even the most sensitive third generation HIV antibody assays and as much as two weeks relative to first generation antibody assays.[40]

GENETIC VARIABILITY

GENETIC VARIABILITY REPRESENTS A DISTINCT CHALLENGE FOR DIAGNOSTIC MANUFACTURERS. The HIV virus exhibits impressive genetic variability, and this variability poses a significant challenge in developing reliable, useful assays that are not fooled by genetic mutations that occur within the HIV genome. According to one estimate, with an average of 10^8 viruses produced daily, virtually every position within the 9.4-kb HIV genome is mutated daily![41] There are reports that during seroconversion, false-negative results, and delayed detection of antibody responses have been observed in infections with HIV-1 non-B subtypes and HIV-2.[42-43] In Europe, the distribution of various HIV subtypes appears to be changing, and there is evidence of the increasing prevalence of HIV-1 group M non-B subtypes (subtypes A and C to J) and HIV-2 infections.[44] While newer assays have been optimized for the detection of HIV-1 group O (Other), group O infections are rare. The significance of HIV-1 group N (New) is uncertain and the success of conventional EIA testing in identifying such infections is unclear.

Despite some degree of immunological cross-reactivity between types and subtypes of HIV, reliable, sensitive detection of the more divergent strains can only be achieved by incorporating specific sequences into assay design. In one study, detection of HIV-2 positive samples by licensed HIV-1 antibody kits ranged from 60% to 91%, depending on the test used.[45] Detection of HIV-1 Group O samples by HIV-1 and HIV-1/HIV-2 assays varied from 0% to 100% in studies with the United States and European tests.[46,47] The challenge to diagnostic manufacturers is to respond to the gradual morphing of the HIV virus, by re-tooling assays as needed to permit them to effectively recognize new strains of the virus.

From a public health perspective, the challenge is to reduce the number of infected individuals who are unaware of their status and unwittingly responsible for spreading the disease. Despite the viruses' potential for mutation and the recognition that assay tuning is important to respond to the dynamics of the HIV epidemic, HIV assays have been quite remarkable in their ability to detect HIV infection. Recently, six FDA-licensed human immunodeficiency virus type 1 (HIV-1) and HIV-1/2 immunoassays, including five enzyme immunoassays and one rapid test, were challenged with up to 250 serum samples collected from various global sites. All six immunoassays detected the vast majority of samples tested. The serum samples were from individuals known to be infected with variants of HIV-1, including group M subtypes A, B, B', C, D, E, F, and G and group O. Only three samples proved problematic, and the authors concluded that HIV-1 immunoassays used in the United States are capable of detecting most HIV-1 group M variants.[48]

Additional Tools: NAAT Tests – Antigen Detection

Nucleic acid amplification testing (NAAT) has been available in the United States as an investigational screening test for donated blood since 1999. In 2002 the FDA approved it for diagnostic purposes. Newer qualitative NAAT systems have been optimized for high-through put, sensitivity and specificity, and are designed and approved for application to individual samples or in mini-pool (MP) testing algorithms.[49] Diagnostic NAAT effectively narrows the window of detection.

Another means to narrow the window of detection is to examine the body fluids for antigens which are present earlier in the infection. Using these approaches it is possible to reduce the period of time to diagnose an HIV infection from approximately 22-24 days (third generation EIAs) to 11-12 days (nucleic amplification tests (NAAT).[8]

The NAAT test is important in a clinical diagnostic setting, and provides the earliest indication of HIV infection, but it is an expensive procedure, and is used much less frequently in the setting of public health screening for HIV infection than it is for diagnostic or patient monitoring. Adding NAAT-based screening to a standard regimen of HIV antibody screening has the potential of identifying people with acute HIV infection earlier in their infection, when they are most infectious and most at risk for transmitting the virus. The acute phase of HIV varies on an individual basis, but usually lasts on average two months. Estimates from studies in Uganda indicate that up to half of all HIV transmissions originate from acutely infected individuals who are unaware of their disease status.[50] Acutely infected persons may be more highly infectious, due to their high HIV viral load, than during other phases of the disease and if they belong to high risk social networks, they may potentiate the risk of transmission.[51-53] The Association of State and Territorial Health Officers reviewed the utility of NAAT screening of antibody-negative specimens from six state and local public health agencies utilizing NAAT to screen pooled specimens for acute HIV infection. All six studies indicated an opportunity to increase the yield over antibody screening alone by between 4 and 11 percent.[54,55]

The NAAT test and the p24 Antigen test identify HIV-1 infections days earlier than antibody testing so they have a clear role in diagnostic testing of risk-exposed individuals. They also have a clear role in clarifying discordant results, i.e., when the initial EIA or rapid HIV test does not agree with the HIV confirmatory assay. However, in terms of screening individuals only modestly at risk for HIV infection, conventional antibody testing is very effective, sensitive and specific.[8]

The APTIMA® HIV-1 RNA Qualitative Assay is a nucleic acid assay system developed by Gen-Probe Inc. (San Diego, California) (www.gen-probe.com) for the detection of HIV-1 in human plasma. Laboratories are currently using qualitative RNA assays to diagnose HIV-1 infection, including acute or primary infection. The presence of HIV-1 RNA in the plasma of patients without antibodies to HIV-1 is indicative of acute or primary HIV-1 infection. The assay has also been approved recently as an additional test, when it is reactive, to confirm HIV-1 infection in an individual whose specimen is repeatedly reactive for HIV-1 antibodies.[8]

In-Office HIV Evaluation

TWO APPROACHES ARE AVAILABLE to the physician: acquiring a specimen and sending it to a commercial laboratory for conventional laboratory testing, or testing at the point-of-care by means of a rapid HIV test. The options available for testing in the point-of-care setting are four FDA-approved CLIA-waived rapid HIV tests.[8] ***(See Table 1)***

Table 1 – FDA-Approved, CLIA-Waived Rapid HIV Tests*

FDA Approved	Manufacturer	Product	Method	Sensitivity	Specificity	HIV2	Waived formats
November, 2002	Orasure Technologies Inc., Bethlehem, PA www.orasure.com	**Oraquick Rapid HIV1/2**	LF	99.6%	100%	Yes	OF WB
December, 2003	Trinity Biotech plc, Bray, Ireland www.unigoldhiv.com	**UniGold Recombinant HIV1**	LF	100%	100%	No	WB
May, 2006	Inverness Medical Professional Diagnostics www.invernessmedicalpd.com	**Clearview HIV 1/2 StatPak**	LF	99.7%	99.9%	Yes	WB
May, 2006	Inverness Medical Professional Diagnostics www.invernessmedicalpd.com	**Clearview HIV 1/2 StatPak**	LF	99.7%	99.9%	Yes	WB

- Beginning in January 2003, the FDA approved and CLIA waived rapid HIV tests for use in various point-of-care settings. To date, all approved tests have utilized a lateral flow immunochromatographic technology. According to their manufacturer submitted data, all had sensitivity in excess of 99.6% and specificity greater than 99.9%.[8]

In the United States, all currently approved, CLIA-waived rapid HIV testing devices are based upon a technology that has been available internationally for more than a decade.[56]

THESE RAPID ASSAYS are available in a kit form that includes all necessary reagents and requires no other specialized equipment. All rapid HIV tests available in the United States utilize a flow-through device made of a hard plastic material that contains a wicking material or membrane inside of it. The HIV antigens are embedded onto this material. All the reagents and the sample are passed through the device, with the sample antibodies binding to corresponding antigens on the membrane. These, in turn, bind a conjugate and a precipitable substrate to allow color development.

In the United States, there are currently four FDA-approved, CLIA-waived, rapid HIV tests utilizing such a format: **Orasure OraQuick, Clearview Stat-Pak, Clearview Complete,** and the **Trinity UniGold.** Internationally, these devices have been in use for many years, and have proven to be rugged and reliable assays. Sensitivity data provided in support of licensure indicates that these assays are at least as sensitive as traditional EIA tests.[8]

The Trinity UniGold HIV-1 product uses recombinant HIV-1 protein antigens rather than peptides in their rapid HIV assay. When IgM or IgG antibodies to HIV-1 are present in the sample, they combine with these proteins and a colored reagent and this complex binds to the proteins in the test forming a visible pink/red band in the test region of the device adjacent to the word "Test."[8]

According to Inverness, the Clearview HIV 1/2 STAT-PAK assay employs a unique combination of a specific antibody binding protein conjugated to colloidal gold dye particles and HIV-1/2 antigens which are bound to the solid phase membrane.[8]

Typically a single-use, rapid HIV test has a retail cost between $14-18, although they are generally available in substantially discounted prices to public health agencies. Although this does not compare favorably to the cost per result available in a high volume clinical laboratory, the overall cost per result to the health system is very favorable since the logistical and labor expenses are dramatically reduced or removed, and the patient expense associated with the follow-up visit is eliminated for more than 95% of the individuals tested.[8]

A number of commercial laboratories provide HIV screening of antibody and antigen detection assays as well as qualitative NAAT services. The antigen and antibody tests generally utilize serum, while NAAT tests routinely utilize frozen plasma. The specimen handling is important in HIV NAAT testing, and physicians' offices should be aware that sample degradation will occur if specimens are not collected properly (white top tube), spun rapidly, and the plasma separated from the cellular constituents of the specimen upon centrifugation and frozen.[8]

HIV Testing Laboratory Licensure Requirements

In New Jersey, two sets of laboratory licensure requirements need to be fulfilled in order to offer rapid HIV testing. These requirements are based on separate federal and New Jersey state regulations.

FEDERAL REGULATIONS: The Centers for Medicare and Medicaid Services (CMS) regulate all laboratory testing performed on humans (with the exception of research). It does so under the auspices of the Clinical Laboratory Improvement Act (CLIA) which originated in 1988. A laboratory is defined under CLIA as "any facility which performs laboratory testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention, treatment of disease or impairment of, or assessment of health.[29]

In 1992, CLIA implemented a methodology based upon the complexity of the lab methodology. They divided laboratory testing into groups classified as either waived, moderate complexity, or high complexity. Waived laboratories must complete an application, enroll in CLIA, pay a fee, become certified and perform testing in accordance with the manufacturer's product insert.[29]

NEW JERSEY STATE REGULATIONS: With the exception of small group practices numbering less than four physicians, clinical group practices and other organizations performing clinical laboratory testing are required to have a State of New Jersey Clinical Laboratory License. The New Jersey regulations recognize only the original CLIA list of waived tests, not the complete list currently waived under federal regulations.[29]

- New Jersey regulations require interested parties to complete an application specifying the procedures to be performed, the personnel performing the procedures, the Bioanalytical Laboratory Director, and also require the laboratories to participate in appropriate proficiency testing.[29]

Conclusion

Changes in HIV testing recommendations, along with the increasing use of rapid, sensitive, and specific HIV screening technology is allowing better integration of HIV testing into routine clinical care. ✦ An advantage of rapid HIV testing is that more patients are receiving their results and are therefore able to act upon the information. ✦ Some of the newer EIA assays and NAAT testing shorten the window period between HIV infection and detection. ✦ As the testing technology changes, new testing strategies will need to be developed. ✦ In conjunction with the APHL, the Centers for Disease Control and Prevention has proposed strategies to confirm a reactive rapid HIV antibody test with a second, different rapid HIV test, thereby eliminating the need for patients to return for confirmatory test results.[13] ✦ This could increase the number of HIV-infected people who know their status and are can be referred earlier for treatment, prevention, and social services. ✦ A pilot project at several publicly-funded HIV counseling and testing sites in New Jersey is verifying each preliminary positive rapid HIV test with a second, different rapid HIV test, followed by immediate linkage to healthcare. For quality purposes, the pilot design includes confirmatory testing (Western Blot) of all positive test results.

HIV Testing Update

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): 1-17.
2. Glynn M, Rhodes P. Estimated HIV Prevalence in the United States at the End of 2003. National HIV Prevention Conference; June 2005; Atlanta. Abstract T1-B1101. Available at: http://www.aegis.com/conferences/NHIVPC/2005/T1-B1101.html. Accessed April 29, 2008.
3. Hall HI, Song R, Rhodes P, et al, for the HIV Incidence Surveillance Group. Estimation of HIV Incidence in the United States. *JAMA,* August 6, 2008:300(5):520.
4. Centers for Disease Control and Prevention: Persons Tested for HIV United States, 2006. *MMWR* 2008,57:845-849.
5. Centers for Disease Control and Prevention. Statistics on Increased Risk for HIV Infection. Available at http://www.cdc.gov/datastatistics/archive/HIV.html. Accessed April 29, 2008.
6. Palella FJ, Deloria-Knoll M, Chmiel JS, et al: Survival Benefit of Initiating Antiretroviral Therapy in HIV-Infected Persons in Different CD4+ Cell Strata. *Ann Intern Med* 2003, 138:620-6.
7. Centers for Disease Control and Prevention. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Healthcare Settings. *MMWR.* 2006;55(RR14):1-17.
8. Paul SM and Martin EG. HIV Test Recommendations, Assay Selection. Advance for Administrators of the Laboratory 2008:17:86-89.
9. Cowan E. The Role of FDA in HIV Testing. Presentation before the Presidential Advisory Council on HIV and AIDS (PACHA). Available at: http://www.pacha.gov/meetings/minutes/m1104.doc. Accessed May 12, 2008.
10. Ng VL. Serological Diagnosis with Recombinant Peptides/Proteins. Clinical Chemistry 1991, 37(10): 1667-1668.
11. Truong HHM and Klausner JD. Diagnostic Assays for HIV-1 Infection. *MLO* 2004, 36 (7): 12-20.
12. Mortimer PP. The Fallibility of HIV Western blot. *Lancet* 1991, 337: 286–287.
13. Paul SM. The 2007 HIV Diagnostics Conference. *New Jersey AIDSLine.* January 2008: 1, 29.
14. Association of State and Territorial Health Officials. Guide to Public Health Practice: HTLV-III Screening in the Community. McLean, VA: Association of State and Territorial Health Officials Foundation; 1985.
15. Centers for Disease Control and Prevention. Advancing HIV Prevention: New Strategies for a Changing Epidemic–United States. MMWR 2003, 52:329-32. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5215a1.htm. Accessed May 14, 2008.
16. Wilson JM and Jungner G. (1968). Principles and Practice of Screening for Disease. Geneva, Switzerland: World Health Organization.
17. Paltiel AD, Weinstein MC, Kimmel AD, et al and the HIV Outpatient Study (HOPS) Investigators: Expanded screening for HIV in the United States – an analysis of cost-effectiveness. *N Engl J Med* 2005:352:586-95.
18. Sanders GD, Bayoumi AM, Sundaram V, et al. Cost-Effectiveness of Screening for HIV in the Era of Highly Active Antiretroviral Therapy. *N Engl J Med* 2005, 352:570-85.
19. Public Health Service Task Force. Recommendations For Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. Available at http://aidsinfo.nih.gov. Accessed April 30, 2008.
20. Centers for Disease Control and Prevention. Pregnancy and Childbirth. Available at: www.cdc.gov/hiv/projects/perinatal. Accessed April 29, 2008.
21. Centers for Disease Control and Prevention. Recommendations to Improve Preconception Health and Healthcare – United States. *MMWR* 2006, 55(No. RR-6). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5506a1.htm. Accessed May 14, 2008.
22. Paul SM and Dimasi LG. New Jersey's New Legislation for HIV Testing of Pregnant Women and Newborns. *New Jersey AIDSLine* June 2008:1, 36.
23. 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. Available at: http://www.cdc.gov/hiv/topics/testing/resources/guidelines/rt-labor&delivery.htm.
24. US Department of Health and Human Services. Antiretroviral Post-Exposure Prophylaxis After Sexual, Injection-Drug Use, or Other Non-Occupational Exposure to HIV in the United States Recommendations from the U.S. Department of Health and Human Services. *MMWR.* 2005:54(RR02):-20. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm Accessed April 14, 2008.
25. Centers for Disease Control and Prevention. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Post-Exposure Prophylaxis. *MMWR* 2005, September 30; 54(RR09):1-17. Available at: http://www.cdc.gov/mmwR/preview/mmwrhtml/rr5409a1.htm. Accessed April 14, 2008.
26. Centers for Disease Control and Prevention. Routinely Recommended HIV Testing at an Urban Urgent-Care Clinic - Atlanta, Georgia 2000. *MMWR* 2001, 50(25):38-541. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5025a3.htm. Accessed April 14, 2008.
27. Centers for Disease Control and Prevention. Update: HIV Counseling and Testing Using Rapid Tests – United States, 1995. *MMWR* 1998, 47; 211-215. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00051718.htm. Accessed April 14, 2008.
28. Centers for Disease Control and Prevention. Update: HIV Counseling and Testing Using Rapid Tests – United States, 1995. *MMWR* 1998; 47; 211-215.
29. Paul SM, Cadoff E and Martin E. Rapid Diagnostic Testing for HIV: Clinical Implications of a New Diagnostic Tool. *New Jersey AIDSLine* 2005:1:3-9.
30. Marks G, Crepaz N, Senterfitt J and Janssen R. Meta-Analysis of High-Risk Sexual Behavior in Persons Aware and Unaware They are Infected With HIV in the United States: Implications for HIV Prevention Programs. *J AIDS* 2005, 39:446-453.

REFERENCES

31. Louie B, Wong E, Klausner JD, et al. Assessment of Rapid Tests for Detection of Human Immunodeficiency Virus-Specific Antibodies in Recently Infected Individuals. Journal of Clinical Microbiology 2008, 46(4): 1494-1497. Available at: http://jcm.asm.org/cgi/content/full/46/4/1494. Accessed May 9, 2008.
32. Constantine NT. Serologic Tests for the Retroviruses: Approaching a Decade of Evolution. *AIDS* 1993, 7:1-13.
33. Zaaijer HL, Exel-Oehlers PV, Kraaijeveld T, Altena E and Lelie PN. Early Detection of Antibodies to HIV-1 by Third-Generation Assays. *Lancet* 1992, 340:770-772.
34. Canna F, Treviño E, Dominguez C, et al. Screening of HIV in Blood Banks. Evaluation of Fourth Generation Kits. *Medicina* (Buenos Aires) 2003, 63(6): 685-691.
35. Weber B, Gürtler L, Thorstensson R, et al. Multi-Center Evaluation of a New Automated Fourth-Generation Human Immunodeficiency Virus Screening Assay with a Sensitive Antigen Detection Module and High Specificity. *J Clin Microbiol* 2002, 40(6): 1938–1946.
36. Abbott Diagnostics Corporation, Package Insert Human Immunodeficiency Virus Types 1 and 2: (E. Coli, B. Megaterium, Recombinant Antigen) - HIVAB™ HIV-1/HIV-2 (DNA) EIA. 2002. Abbott Diagnostics Division, Abbott Park, IL 60064.
37. Lyons J, Margolin F, Lampe M and Branson B. Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays – A Summary of Manufacturer Inserts. Available at: http://www.hret.org/hret/programs/content/elisachart.pdf. Accessed May 12, 2008.
38. Busch MP, Kleinman SH, Jackson B, Stramer SL, Hewlett J and Preston S. Committee Report. Nucleic Acid Amplification Testing of Blood Donors for Transfusion-Transmitted Infectious Diseases: Report of the Inter-Organizational Task Force on Nucleic Acid Amplification Testing of Blood Donors. *Transfusion* 2000, 40:143-159
39. Berrey MM, Schlaker T, Collier AC, et al. Treatment of Primary Human Immunodeficiency Virus Type 1 Infection with Potent Antiretroviral Therapy Reduces Frequency of Rapid Progression to AIDS. *J. Infect. Dis.* 2001. 183:1466-1475.
40. Devare SG. Early Diagnosis of HIV Infection. *J. Med. Virol.* 2007, 79:S11-S15.
41. Subbarao S, Schochetman G. Genetic Variability of HIV-1. AIDS 1996, 10 (Suppl. A):S13–S23.
42. Christiansen CB, Jessen TE, Nielsen S, and Staun-Olsen P. False Negative Anti-HIV-1/HIV-2 ELISAs in Acute HIV-2 Infection. *Vox Sanguis*. 1996, 70:144-147.
43. Apetrei C, Loussert-Ajaka I, Deschamps D, et al. Lack of Screening Test Sensitivity During HIV-1 Non-Subtype B Seroconversions. *AIDS* 1996, 10:57-60.
44. Simon F, Mauclere P, Roques P, et al. Identification of a New Human Immunodeficiency Virus Type 1 Distinct from Group M and Group O. *Nat. Med* 1998, 4:1032-1037.
45. George JR, Rayfield M, Phillips S, et al. Efficacies of U.S. FDA Licensed HIV-1 Screening Enzyme Immunoassays for Detecting Antibodies to HIV-2. *AIDS* 1990, 4:321-326.
46. Loussert-Ajaka I, Ly TD, Chaix ML, et al. HIV-1/HIV-2 Seronegativity in HIV-1 Subtype O Infected Patients. *Lancet* 1994, 343:1393-1394.
47. Schable C, Leopold Z, Pau CP, et al. Sensitivity of United States HIV Antibody Tests for Detection of HIV-1 Group O Infections. *Lancet* 1994, 344:1333-1334.
48. Koch WH, Sullivan PS, Roberts C, et al. Evaluation of United-Licensed Human Immunodeficiency Virus Immunoassays for Detection of Group M Viral Variants. *J Clin Microbiol.* 2001, 39(3): 1017–1020. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=87866#B25. Accessed May 8, 2008.
49. Busch MP and Hecht FM. Nucleic acid amplification testing for diagnosis of acute HIV infection: has the time come? *AIDS* 2005, 19:1317-1319.
50. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 Transmission Per Coital Act, by Stage of HIV-1 Infection, in Rakai, Uganda. *J. Infect Dis.* 2005, 191:1403-1409.
51. Koopman JS, et al. The Role of Early HIV Infection in the Spread of HIV through Populations. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1997; 14:249-258.
52. Pilcher CD, et al. Brief but Efficient: Acute HIV Infection and the Sexual Transmission of HIV. *J Infect Dis* 2004, 189(10): 1785-1792.
53. Feibig EW, et al. Dynamics of HIV Viremia and Antibody Seroconversion in Plasma Donors: Implications for Diagnosis and Staging of Primary HIV Infection. *AIDS.* 2003; 17:1871-1879.
54. Pilcher CD, et al. Detection of Acute Infection During HIV Testing in North Carolina. *N Engl J Med* 2005, 352(18):1873-1883.
55. Patel P, Klausner JD, Bacon OM, et al. Detection of Acute HIV Infections in High-Risk Patients in California. *J Acquir Immune Defic Syndr.* 2006, 42(1): 75-9.
56. Granade T. Rapid HIV Testing Techniques. 1998 Conference on the Laboratory Science of HIV. Available at: http://wwwn.cdc.gov/mlp/pdf/labhiv/TGranade.pdf. Accessed May 5, 2008.

Resources: Rapid HIV Testing

AT YOUR HEALTH CARE SITE:

- Free 1-hour HIV medical education program on Rapid HIV Testing!
  To schedule, contact Michelle Thompson at (973) 972-1293 or ccthomps@umdnj.edu

ON THE WEB:

- NJDHSS-DHAS website: New Jersey-specific FAQs (frequently asked questions), updated Rapid Test site locations, laboratory regulations, and links: www.state.nj.us/health/aids/rapidtesting/index.shtml
- New Jersey HIV Rapid Testing Website: laboratory information for NJ Point of Care Testing (POCT): http://njhiv1.org
- CDC Rapid HIV Testing website: updated Rapid Test counseling and laboratory guidelines, official CDC and FDA releases, package inserts, CLIA regulations, and research reports: www.cdc.gov/hiv/rapid_testing

CE
CONTINUING EDUCATION

HIV Testing Update

Post-Test – Page 1 of 1

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. **A positive result on a rapid HIV test should be considered preliminary. What is the standard, reliable confirmatory test?**
   A. $CD4^+$ test
   B. Genotypic test
   C. Phenotypic test
   D. Western blot

2. **When should the p24 antigen test be used to confirm HIV-1 infection following a positive EIA?**
   A. The patient has requested post-exposure prophylaxis following unprotected sexual activity with a partner whose HIV status is unknown.
   B. The patient is the sexual partner of an HIV patient.
   C. The patient has discordant test results, e.g., positive EIA and negative Western Blot.
   D. The EIA was performed on an anonymous basis, and the clinic requires documentation of HIV infection before providing HIV care.

3. **Which of the following healthy patients should have HIV screening as part of routine medical care?**
   A. A Pregnant woman in first trimester.
   B. A 23-three-old with no known risk factors.
   C. A 60-year-old with no known risk factors.
   D. All of the above.

4. **The 2006 CDC recommendations for opt-out HIV testing includes which of the following?**
   A. A separate signed consent form for HIV testing.
   B. A separate signed declination form for HIV testing
   C. Consent included in the general consent form for medical care.
   D. No verbal or signed consent form.

5. **A false negative result on an HIV EIA (Enzyme Immunoassay) is most often due to:**
   A. Conducting the test during the "window period" before adequate antibodies have developed.
   B. Defective test.
   C. Epstein-Barr virus.
   D. Multiple pregnancies.

6. **Which of the following persons should not be offered a rapid HIV test to reduce the risk of transmission?**
   A. Man who presents with a sexually transmitted disease.
   B. Routine office visit for a patient with a history of injection drug use.
   C. Ward clerk on a unit that has an HIV infected patient.
   D. Woman in labor with unknown HIV status.

7. **Which of the following is an exception to the need for a laboratory license from the New Jersey Department of Health and Senior Services to conduct rapid HIV testing?**
   A. Hospitals.
   B. Federally Qualified Health Care Centers.
   C. Physician practices with less than four physicians.
   D. New Jersey Department of Health and Senior Services funded counseling and testing site.

8. **Rapid HIV Testing has demonstrated sensitivity of 99.6% ad specificity of 99.8%. How do rapid tests compare with conventional EIA tests?**
   A. Inferior to the specificity and sensitivity of current, 3rd-generation EIA tests.
   B. Equivalent to a conventional 3rd-generation EIA.
   C. Equivalent to first generation EIAs still in use in many laboratories.
   D. Superior to conventional 3rd-generation EIA.

9. **Which of the following should be included in the posttest counseling session for a patient with a preliminary positive (reactive) rapid diagnostic HIV test?**
   A. Information on additional laboratory tests (i.e., viral load and CD4 T cell tests).
   B. Obtaining a list of contacts who need to be informed of their potential HIV exposure.
   C. Referral to a physician with experience and expertise treating HIV disease.
   D. Explain that he/she is highly likely to be infected with HIV and a second confirmatory test is required.

10. **Which of the following is an advantage of rapid diagnostic HIV testing?**
    A. Increases the likelihood that a patient will seek HIV counseling and testing.
    B. Increases the number of patients who receive their HIV results.
    C. Increases the proportion of HIV infected patients who enter treatment.
    D. Increases adherence to antiretroviral therapy in HIV infected patients.

CE Activity Code: 110HC02- DE01

CONTINUING EDUCATION

HIV Testing Update
Registration Form

CCOE
Center for Continuing & Outreach Education

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)™* 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.

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.umdnj.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 *Circle the best answer for each question.*	**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

– PLEASE PRINT –

First Name _____ M.I. _____ Last Name _____ Degree _____

Daytime Phone # _____ Evening Phone # _____

Fax # _____ E-mail _____

Preferred Mailing Address: ☐ Home ☐ Business

Address _____

City _____ State _____ Zip Code _____

Affiliation/Specialty _____

Indicate the type of continuing education credit you with to obtain as a result of your participation in this activity.

☐ **Nurses:** Nursing contact hours (ANCC): Hours awarded: 1.25

☐ **Physicians**: *AMA PRA Category 1 Credit(s)™* Credit Letter: Credits Claimed: _____

☐ **General:** Continuing Education Units (up to 0.125): 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.

Signature _____ Date _____

Release date: January 2009 • **Expiration date:** Credit for this activity will be provided through June 30, 2010.
Nursing Credit for this activity will be provided through June 30, 2010.

UMDNJ-Center for Continuing & Outreach Education
PO Box 1709, Newark, New Jersey 07101-1709
Phone: 973-972-4267 or 1-800-227-4852 • Fax: 973-972-7128

CE Activity Code: 11HC02- DE01
This form may be photocopied.

CE
CONTINUING EDUCATION

HIV Testing Update

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.

CCOE
Center for Continuing & Outreach Education

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form. Thank you for your cooperation!

PROGRAM OBJECTIVES:		**Strongly Agree**				**Strongly Disagree**
Having completed this activity, are you better able to:						
Objective 1:	Describe the most recent Centers for Disease Control and Prevention recommendations for HIV testing.	5	4	3	2	1
Objective 2:	Explain the indications for rapid HIV testing of women in labor and some newborns.	5	4	3	2	1
Objective 3:	Describe the licensing requirements for rapid HIV testing.	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:

CE Activity Code: 11HC02- DE01
This form may be photocopied.

Prior Authorization Required for Second Line HIV Medications in New Jersey

(Continued from front page)

Treatment Recommendations

While the FDA has approved 32 antiretroviral agents in five classes, they are not all approved for use in the initial treatment of HIV/AIDS. Antiretroviral treatment failure (a suboptimal response to treatment) is not uncommon, and it increases the risk for HIV disease progression. Treatment failure needs to be addressed aggressively.[3] One of the greatest challenges for clinicians is managing treatment-experienced patients, or those who have developed resistance to multiple classes of antiretroviral agents. Cross-resistance within classes of antiretroviral agents has driven development of the newest classes of antiretroviral agents: entry inhibitors, fusion inhibitors, and integrase inhibitors.[4]

In selection of a combination of antiretroviral agents, the sequence of drugs is important. Current recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents indicate that patients with treatment failure should ideally be placed on a new or "salvage" regimen, with at least two, and preferably three, fully active drugs on the basis of drug history, resistance testing, or new mechanistic class.[3] The new agents that are FDA-approved specifically for use by treatment-experienced patients only offer options for replacing antiretroviral agents that are no longer working for that patient.[4]

Antiretroviral Agents Needing Prior Approval in New Jersey

The New Jersey Department of Health and Senior Services (NJDHSS), Division of HIV/AIDS Services (DHAS) identified a need for prior authorization for antiretroviral agents that are not approved by the Food and Drug Administration (FDA) as first-line medications for the treatment of HIV/AIDS. The inappropriate use of these "salvage" medications as first-line medications could lead to resistance, thereby making them ineffective for use by treatment-experienced patients who are on a failing regimen.

The following antiretroviral agents should be reserved for treatment-experienced patients, and are not currently FDA approved for the initial treatment of HIV disease. Their use now requires a prior approval process for patients receiving publicly funded medications in New Jersey.

- Enfuvirtide (Fuzeon) – (See Figure 2 on page 31)
- Etravirine (Intelence) – (See Figure 3 on page 31)
- Maraviroc (Selzentry) – (See Figure 4 on page 32)
- Raltegravir (Isentress) – (See Figure 5 on page 32)
- Tipranavir (Aptivus) – (See Figure 6 on page 33)

The Prior Authorization Process

Prior Authorization (PA) criteria are based on FDA-approved indications, the approval of the New Jersey Drug Utilization review Board (DURB), and as well as peer-reviewed medical literature. PA is a paperless process that occurs in real-time at the pharmacy where claims are processed. It occurs instantaneously and it does not require anyone to enter PA numbers.

The process begins when a licensed prescriber writes a prescription for Enfurvatide, Etravirine, Maraviroc, Raltegravir, or Tipranavir. The patient gives the prescription to a pharmacist. When the pharmacist enters the prescription into the computer, the system link to the Unisys system (NJMMIS) will indicate that a PA is required.

(Continued on next page)

The point-of-sale pharmacist reviews the patient's drug profile BEFORE he/she calls the Medical Exception Program (MEP) to inform them that a physician is requesting one of the second line HIV medications.

The "HIV Team" of the MEP, located in UNISYS, includes a cadre of pharmacists and nurses, whose specialized focus area is HIV. The pharmacist provides as much information as possible to the MEP "HIV Team" member. The MEP initiates the paperless prior authorization process. A MEP HIV Team Member will call the physician if more specific information is needed. The MEP HIV "Team Member" bases his/her decision on the information provided by the pharmacist, the UNISYS claims history data-bases, and a standardized algorithm. The MEP HIV "Team Member" will communicate back to the pharmacy with the decision to approve or deny the PA. If the PA is approved, the medication is dispensed. The timing varies from a few minutes if it is not necessary to call the physician to verify the regimen or discuss a drug-drug interaction to a longer time frame when a MEP HIV Team Member needs to speak with a physician. If it is a renewal, the pharmacist will call the MEP. If there are no new drug-related issues, the PA will be completed within minutes. If a new adverse drug-drug interaction is detected, the MEP may need to call the physician.

Figure 1 is the algorithm depicting the PA process from the time of receipt of the prescription for antiretroviral agents at the pharmacy to the final step of dispensing the medication following approval.

The algorithms, approved by the DURB for use by the MEP HIV "Team Member" for each of the second line antiretroviral agents, are included in this article in Figures 2 to 6.

2nd Line HIV Medications

The following antiretroviral agents should be reserved for treatment-experienced patients, and are not currently FDA approved for the initial treatment of HIVdisease. Their use now requires a prior approval process for patients receiving publicly funded medications in New Jersey.

Providers needing further assistance from the "HIV" Team at the Medical Exception Program located in UNISYS may call the toll free number 877-888-2939.
(See page 33 for more information.)

FIGURE 1

Prior Authorization (PA) Process

Algorithm for 2nd Line/Salvage HIV Medications

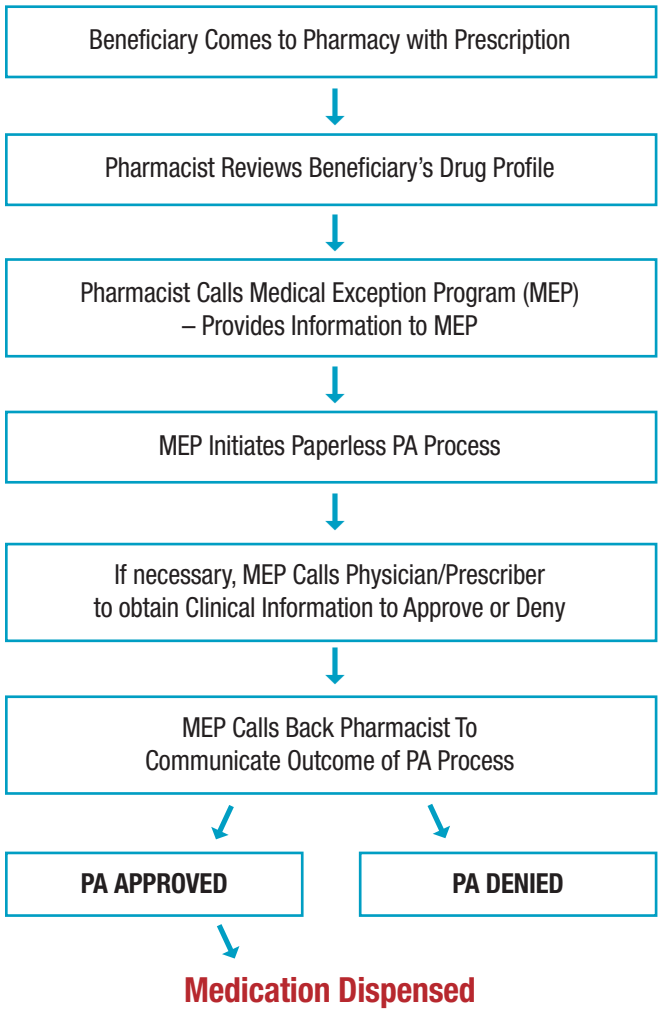


FIGURE 2
Eligibility Criteria for Fuzeon

1. Is this patient currently receiving Fuzeon via an expanded access program? *(If yes, approve Fuzeon. If no, proceed to question 2.)*
   ☐ YES ☐ NO

2. Has the patient been on antiretroviral agents in the past?
   (If yes, proceed. If no, stop, not eligible for Fuzeon.)
   ☐ YES ☐ NO

3. Is there evidence of viral replication despite ongoing antiretroviral therapy, and viral load greater than 1,000 copies/ml, with a second confirmatory test? *(If yes, proceed. If no, stop, not eligible for Fuzeon.)*
   ☐ YES ☐ NO

4. Has a recent HIV resistance test been conducted and ARV history reviewed to determine an optimal base regimen of at least two active and tolerated ARVs and to eliminate inactive ARVs?

   OR

   Will Fuzeon be used as part of an alternative salvage regime for a patient with end-stage disease who is at risk of serious Opportunistic Infections or death? *(If yes, proceed. If no, stop, not eligible for Fuzeon.)*
   ☐ YES ☐ NO

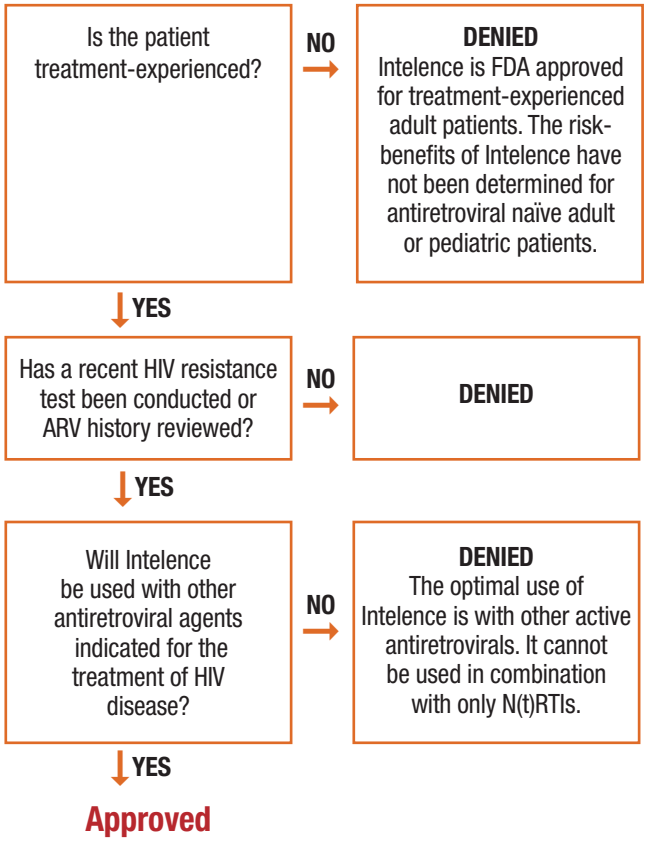
5. Has the patient kept ≥ 4 of their appointments in the past 12 months or has the patient been reliable in keeping their appointments and do you think this patient will adhere to a Fuzeon containing regimen?
   (If yes, proceed. If no, stop, not eligible for Fuzeon.)
   ☐ YES ☐ NO

6. Is your office willing to accept shipments of Fuzeon?
   (If yes, proceed. If no, stop, not eligible for Fuzeon because the provider cannot accept shipment. The patient may be eligible if they have another provider who can accept shipment.)
   ☐ YES ☐ NO

7. Can the patient or his/her primary care giver reconstitute and administer the subcutaneous injections b.i.d. and properly dispose of the used syringes and needles? *(If yes, proceed. If no, stop, not eligible for Fuzeon.)*
   ☐ YES ☐ NO

8. Is the patient up to date on pneumococcal and influenza immunizations? *(If not, please ensure that the patient is appropriately immunized. Eligible for Fuzeon regardless of response.)*
   ☐ YES ☐ NO

FIGURE 3
Intelence (etravirine)
Prior Approval Algorithm



The algorithms, approved by the DURB for use by the MEP HIV "Team Member" for each of the second line antiretroviral agents, are included in Figures 4 to 6.

FIGURE 4
Selzentry (Maraviroc)
Prior Approval Algorithm

- Is the patient treatment-experienced?
  - NO → **DENIED** Selzentry is FDA approved for treatment-experienced patients. There are no studies in antiretroviral naïve patients.
  - YES ↓
- Has a recent HIV resistance test been conducted or ARV history reviewed?
  - NO → **DENIED**
  - YES ↓
- Is there evidence of antiretroviral resistance in two or more drug classes that resulted in incomplete HIV suppression?
  - NO → **DENIED**
  - YES ↓
- Has a tropism test been conducted and has the virus been demonstrated to be CCR5-tropic?
  - NO → **DENIED** Selzentry is FDA approved for patients with CCR5-tropic HIV1 detectable virus only.
  - YES ↓
- Will Maraviroc be used with other antiretroviral agents indicated for the treatment of HIV disease?
  - NO → **DENIED**
  - YES ↓

Approved

FIGURE 5
Isentress (Raltegravir)
Prior Approval Algorithm

- Is the patient treatment-experienced?
  - NO → **DENIED** Isentress is FDA approved for treatment-experienced adult patients. The risk-benefits of Isentress have not been determined for antiretroviral naïve adult or pediatric patients.
  - YES ↓
- Has a recent HIV resistance test been conducted or ARV history reviewed?
  - NO → **DENIED**
  - YES ↓
- Will Isentress be used with other antiretroviral agents indicated for the treatment of HIV disease?
  - NO → **DENIED** The optimal use of Isentress is with other active antiretrovirals.
  - YES ↓

Approved

REFERENCES

1. National Institutes of Health. Treatment of HIV Infection. Available at http://www.niaid.nih.gov/factsheets/treat-hiv.htm. Accessed May 13, 2008.
2. United States Food and Drug Administration. Drugs use in the Treatment of HIV Infection. Available at http://www.fda.gov/oashi/aids/virals.html Accessed May 14, 2008.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. November 3, 2008; 1-139. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed December 22, 2008.
4. Kaur A and Paul S. Role of Newly-Approved Antiretroviral Agents in Treatment-Experienced Patients. *New Jersey AIDSLine*, January 2008:3-7.

FIGURE 6
Tipranavir (Aptivus)
Prior Approval Algorithm

Is the patient allergic to ritonavir (Norvir) or Sulfa drugs?
- YES → **DENIED**
- NO ↓

Is the patient treatment-experienced?
- NO → **DENIED** Aptivus is FDA approved for treatment-experienced patients. The risk-benefits of Aptivus/ritonavir have not been determined for antiretroviral naive patients.
- YES ↓

Is there evidence of viral replication despite ongoing antiretroviral therapy and resistance to multiple protease inhibitors?
- NO → **DENIED** Due to toxicity and limited clinical data Aptivus should be reserved for patients for whom viral suppression is incomplete with other antiretroviral regimens.
- YES ↓

Has a recent HIV resistance test been conducted and ARV history reviewed, to determine an optimal base regimen of at least two active and tolerated ARVs and to eliminate inactive ARVs?
- NO → **The optimal use of Aptivus is with at least two other active antiretrovirals.**

  Will Aptivus be used as part of an alternative salvage regime for a patient with end-stage disease who is at risk of serious Opportunistic Infections or death?
  - NO → **DENIED** Proposed use of Aptivus in this patient is not end-stage salvage, and is not optimal use with two other active ARVs as defined by clinical trial data.
  - YES ↓
- YES ↓

Aptivus/Ritonavir has been associated with reports of clinical hepatitis and hepatic decompensation, including fatalities. Have liver function tests been performed prior to the initiation of therapy and scheduled frequently during the course of treatment?
- YES ↓

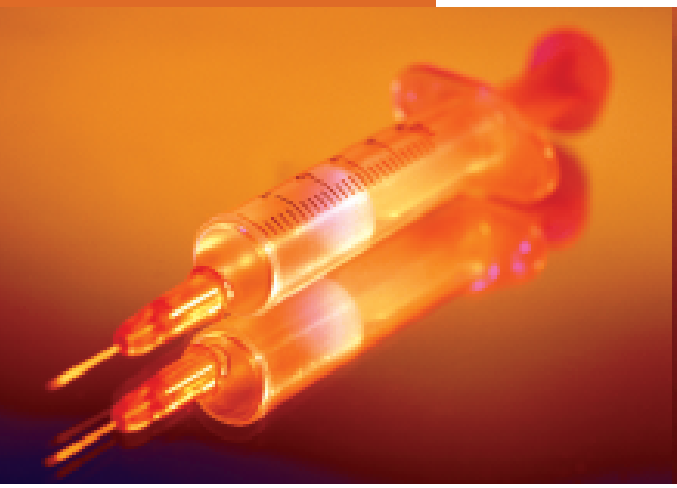
Due to the high dosage and cost of the ritonavir (Norvir), ADP requires that ritonavir, for co-administration with Aptivus, be obtained for free from Abbott Laboratories' Patient Assistance Program by calling 1-800-222-6885 or using the on-line application available at www.rxabbott.com.
- YES ↓

Approved

Contact Number for Further Information Toll-free 877-888-2939

Providers needing further assistance from the "HIV" Team at the Medical Exception Program located in UNISYS may call the toll free number 877-888-2939. During normal business hours, from 8 a.m. to 5 p.m. Monday through Friday, a MEP program professional will answer the call. After business hours and holidays, an answering service will facilitate communication with the "on call" MEP HIV "Team Member."

NEW JERSEY AIDSLine January 2009



STERILE SYRINGE ACCESS Program (SSAP) Established in New Jersey

Rawan Allozi,[1] *Sindy M. Paul, MD, MPH, FACPM,*[2] *Kristy Lento,*[3] *Tefera Gezmu, MPH*[3] *and Kitaw Demissie, MD, PhD*[3]

[1] Washington University, St. Louis (student) • [2] New Jersey Department of Health and Senior Services • [3] UMDNJ-School of Public Health

On October 20, 2006, the 212th Legislature of the state of New Jersey passed the "Bloodborne Disease Harm Reduction Act" permitting the establishment of a demonstration sterile syringe access program (SSAP) in New Jersey. This law permits injection drug users (IDUs), 18 years of age or older, to have access to clean syringes and needles in six major cities of New Jersey. In conjunction with the law, the state of New Jersey also appropriated ten million dollars for drug treatment programs.

The main goal of the SSAPs is to reduce the transmission of bloodborne pathogens, such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), through the sharing of contaminated syringes and needles by injection drug users.[1]

THE SSAPS ACHIEVE THIS GOAL BY:

- Providing access to sterile syringes and needles for IDUs at no cost to the individual;
- Offering additional services which enhance participants' knowledge about:
  - –Methods for safe and proper disposal of needles and syringes as well as encouraging them to return used syringes and needles;
  - –Safe sex practices;
  - –Counseling, and referral services for programs that are relevant to participant health, housing, social service, employment, and other needs.
- Providing IDUs with direct access to drug treatment programs through referral.[2]

SEVERAL GOVERNMENT-COMMISSIONED COMMITTEES, as well as scientific and professional organizations including the National Commission on AIDS, the U.S. General Accounting Office, the Centers for Disease Control and Prevention, and the National Academy of Sciences, have evaluated the effectiveness of SSAPs. Collectively, the findings support the beneficial effects of the SSAPs and have not found negative outcomes.[3] Similarly, the SSAPs have been endorsed independently by several scientific and professional bodies, including the National Institutes of Health Consensus Panel (NIHCP), the American Public Health Association, the American Medical Association, the National Academy of Sciences, and the American Academy of Pediatrics.

When compared with other states, New Jersey has among the highest proportion of women (35%) among people living with HIV/AIDS, and ranks fifth in the nation in terms of cumulative AIDS cases and third in cumulative pediatric AIDS cases.[4]

The NJDHSS surveillance report in June 2008 reported that among the 35,309 people living with HIV/AIDS in New Jersey:

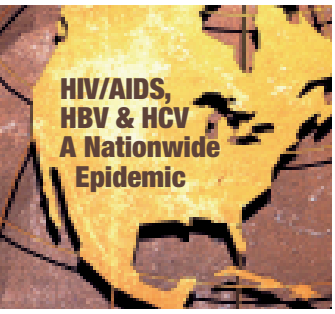
- **26%** had HIV exposure through IDU.
- An additional **5%** via heterosexual transmission from an IDU.
- **2%** were men who had sex with men (MSM) who also were IDUs.
- **33%** had infections that were related to injection drug use.

This is in contrast to national rates of 26% IDU among women living with HIV/AIDS, and 17% among men, as well as 7% of men who had transmission attributed to risks of both IDU and sex with men.[4,5,8]

Prior to the implementation of the current demonstration program, New Jersey remained one of the two states in the nation without an SSAP, despite the above statistics demonstrating the significance of injection drug use in HIV infection.

HIV/AIDS, HBV, and HCV: A Nationwide Epidemic

HIV/AIDS



Since the first case of HIV was reported in 1981, more than 1.7 million people in the United States have been infected with HIV, and more than 550,000 have become victims of AIDS. The Centers for Disease Control and Prevention (CDC) estimates that approximately 56,300 people in the United States became infected with HIV in 2006.[4,9] Today, in the third decade of the HIV/AIDS epidemic, an estimated 1.2 million people are living with the disease. Although a vaccine or cure has yet to be found, great advances have been made to combat this disease.[4]

In 1995, HIV was the leading cause of death for those 25 to 44 years of age; however, due to the advent of highly active antiretroviral therapy (HAART), the HIV mortality rate declined by approximately 70% between 1995 and 2002. In 2003, this decrease caused HIV to no longer be the leading cause of death in the United States, dropping to the sixth leading cause of death.[4] In addition, improved treatment options increased the number of those living with HIV/AIDS by 27%, from 331,482 in 2001 to 421,873 in 2005.[10] Nonetheless, approximately 25% of those infected with HIV are not aware of their diagnosis, and 42% to 59% of those infected do not receive any care.[11]

The following is based on 2006 CDC data obtained from the 33 states with long-term, confidential, name-based HIV/AIDS reporting:

- Men accounted for **73%** of HIV/AIDS cases. Of these cases, **67%** resulted from MSM, **16%** from heterosexual contact, **12%** from IDU, and **5%** from IDU and MSM.
- Women once accounted for only **8%** of the total HIV cases. However, this number increased to **25%** in 2006. Of these cases, **80%** resulted from heterosexual contact and approximately **19%** from IDU.
- In addition, of those living with HIV/AIDS in 2006, **49%** were Black, **30%** were White, and **18%** were Hispanic.[12]

HCV

Hepatitis C, caused by HCV, occurs when the blood from an infected person contaminates the blood of another who is not infected. The routes of transmission are similar to that of HBV, including sexual intercourse, mother to infant, sharing contaminated needles and/or syringes and needle sticks. Those at high risk of HCV infection include IDUs, recipients of clotting factors made before 1987, hemodialysis patients, recipients of blood and/or solid organs before 1992, people with undiagnosed liver disease, infants born to infected mothers, healthcare and public safety workers, people having sex with multiple partners, and people having sex with an infected steady partner. Consequently, those at risk for HCV are also at risk for HIV and HBV.[14]

According to the CDC, an estimated 4.1 million Americans have been infected with HCV, and 80% have no signs or symptoms. It is estimated that there are 26,000 new infections in the United States each year. Chronic HCV infection occurs in 75% to 85% of those infected, and chronic liver disease occurs in 60-70%.[11] One-fourth of those infected with HIV are also infected with HCV. HCV causes a much more rapid onset of liver damage in those who are co-infected, and also impacts the course of HIV infection.[4]

Currently, there is no vaccine available to prevent infection by HCV. Interferon, pegylated interferon, and ribavirin are FDA approved for treatment of hepatitis C. Combination therapy with pegylated interferon/ribavirin is the preferred regimen.

HBV

Hepatitis B is a disease caused by HBV, which attacks the liver, and occurs when the blood from an infected person contaminates the blood of another who is not infected. It is further spread by having sex with an infected person without using a condom, from an infected mother to her infant, or as a result of sharing contaminated needles and/or syringes and through needle sticks. Those at risk of contracting HBV include: MSM, those with multiple sex partners, IDUs, infants born to infected mothers, children of immigrants from areas with high rates of HBV, healthcare and public safety workers, and hemodialysis patients. Consequently, those at risk for HBV are also at risk for HIV and HCV.[13]

Approximately 30% of those infected with HBV have no signs or symptoms, and signs and symptoms are even less common in children than in adolescents and adults. Only 5% to 10% of those infected adults go on to develop chronic HBV infections. Death from chronic liver disease occurs in 15% to 25% of those chronically infected and drinking alcohol may worsen liver disease.

A safe and effective HBV vaccine that prevents the disease and its serious consequences has been available since 1982, with routine vaccinations recommended for those 0 to 18 years of age. The vaccine is synthesized by saccharomyces cerevisiae (common bakers' yeast), into which a plasmid containing the gene for HBsAg is inserted, so those allergic to yeast should not be vaccinated. Persons infected with HBV should be treated with adefovir dipivoxil, interferon alfa-2b, pegylated interferon alfa-2a, lamivudine, entecavir, or telbivudine. These drugs should not be used by pregnant women.

HIV/AIDS, HBV, and HCV in New Jersey

HIV/AIDS

In the past two decades, over 70,000 residents of New Jersey have been diagnosed with HIV/AIDS. Transmission via intravenous drug use has accounted for the largest proportion of HIV/AIDS cases in New Jersey, including 39% of cumulative cases, compared to national reports of 14% of cases attributable to IDU.[12]

In 2008 New Jersey surveillance reports, a total of 33% of cases of AIDS were attributable to injection drug use, either directly (26%), a combination of IDU with MSM (men who have sex with men) (2%), or heterosexual contact with an IDU (5%).[7,15]

New Jersey cases associated with transmission between men who have sex with men (MSM) accounted for 20% of cases, versus 37% of national cases. An additional 3% of all New Jersey cases, or 5% of male cases of AIDS, were attributable to both IDU and MSM, versus 4% of the total and 5% of male AIDS cases nationally.[12]

HIV/AIDS has had disproportionate impact by race and ethnicity. In 2005, in New Jersey, 64% of the population was White, 15% was Hispanic, 14% was Black, 7% was Asian and 0.2% was Alaska Native/Native American. Among the New Jersey residents living with HIV/AIDS, 55% were Black, 22% were Hispanic, and 22% were White. In addition, 76% were 40 years of age or older.[7] As of December 2007, 1 in 63 Blacks, 1 in 183 Hispanics, and 1 in 728 Whites were living with HIV/AIDS.[7] HIV is the leading cause of death for Blacks 25 to 44. While HIV is the 14th leading cause of death for men in New Jersey, it is the 3rd leading cause of death for Black men. Furthermore, while HIV is the 18th leading cause of death for all women in New Jersey, it is the 6th leading cause of death for Black women. Statistics on the rate of progression from HIV to AIDS show that Black and Hispanic patients progressed to AIDS faster than Whites, which may be due in part to poorer access to health care.[4]

In New Jersey, 31% of HIV/AIDS cases are among women, which is one of the highest rates in the US, compared to the national rate of 26%.[7,12] Again, minorities are disproportionately affected. In 2007, Black women accounted for 64% of HIV/AIDS cases among New Jersey women, Hispanic women accounted for 19%, and White women accounted for 16%.

The counties of Passaic, Bergen, Hudson, Union, Essex, Middlesex, Monmouth, Mercer, Camden, and Atlantic account for 83.4% of HIV cases in New Jersey. The largest number of cases occurs in Essex, where 1 in 85 residents is infected, and Hudson, where 1 in 140 residents is infected. The highest numbers of cases occur in the cities of Newark, Jersey City, Paterson, East Orange, Elizabeth, Trenton, Irvington, Atlantic City, Camden, and Plainfield. The largest number of cases among Blacks occurs in Atlantic City, where 1 in 31 residents is infected, and Newark, where one in 33 residents is infected.[4]

HBV

In the United States, the overall number of new HBV infections per year has decreased by about 200,000 cases, from approximately 260,000 in the 1980s, to an estimated 60,000 in 2004. Since the late 1980s, New Jersey followed the same trend and the incidence of HBV appeared to be decreasing; however, in recent years these numbers have significantly increased. From 2000 to 2006, the number of newly reported cases of HBV in New Jersey rose from 179 to 1,478.[16]

HCV

Hepatitis C only became a reportable disease a decade ago, but since then the number of reported cases has continued to rise. The CDC estimates that 1.8% of people in the United States are infected with HCV, which would translate to approximately 155,000 New Jersey residents. In New Jersey there were 4,949 cases of newly diagnosed HCV reported in 2006.[17] It is believed that these numbers do not reveal the true magnitude of this epidemic, as HCV tends to be greatly underreported and under-diagnosed. There is also extremely limited information available on patient characteristics and treatment information for most reported cases in New Jersey.

History of SSAPs

The first SSAP in the world was established in 1984 in Amsterdam, the Netherlands, by a drug user's advocacy group in an effort to prevent the tolling HBV epidemic. In the United States, SSAPs began after the first United States AIDS cases were reported in June of 1981, and the subsequent AIDS epidemic took its toll on the United States. The first illegal operation was run in 1986 by Jon Parker, who distributed syringes and needles on the streets of New Haven and Boston. In 1988, the first legal program was established in Tacoma, Washington.[24]

SSAPs in Practice

SSAP Studies

Many scientific studies have been conducted in an effort to evaluate the SSAPs and address the concerns presented by parties that oppose the implementation of these programs. As summarized by Vlahov and Junge,[3] evidence for the effectiveness of the SSAPs came from three sources: 1) studies that originally evaluated the effectiveness of SSAPs in non-HIV bloodborne infections, (2) mathematical modeling studies on the effectiveness of SSAPs on HIV seroconversion, and (3) studies that directly examine the impact of SSAPs on HIV and AIDS.

Observational studies, in particular, case-control studies have provided strong evidence on the effectiveness of SSAPs in reducing the transmission of HBV and HCV infections. Non-use of SSAP is associated, respectively, with a six-fold and a seven-fold increased risk in HBV and HCV infections among IDUs.[25] A more recent study reviewed 18 papers on evidence for the effectiveness of primary prevention interventions for HCV among IDUs and concluded that SSAPs reduce the prevalence of HCV.[26] These results suggest that the SSAPs lead to a reduction in HBV and HCV infections in the United States.

Among IDUs, non-use of SSAP is associated with an increased risk of six fold for HBV and seven fold for HCV.[25]

SSAPs in Practice

IDUs in New Jersey

Data from the 2004 National Household Survey on Drug Use, as well as data obtained from two studies using capture-recapture analysis for drug treatment admissions, indicates that there are approximately 152,312 to 171,000 IDUs in New Jersey.[18,19,30] Essex County contributed the largest statewide estimated number of IDUs, followed by Camden, Burlington, Hudson, and Monmouth Counties. These estimates are likely to be an underestimate as all drug data from the National Household Survey on Drug Use are self-reported, and some participants maybe reluctant to disclose this behavior. That survey also excludes prisoners and homeless people who are not living in shelters, groups which have high rates of drug use.[21,22,23] Prevalence estimates of IDUs from drug treatment data are assumed by researchers to underestimate the true number of IDUs in the population.

A more recent review of the literature on the effectiveness of SSAPs concluded that there is substantial evidence that the SSAPs are effective in preventing HIV risk behavior and HIV seroconversion among IDUs. The review, by Gibson et al, included 42 published studies conducted in the United States, Canada, and the Netherlands. Twenty-eight found beneficial effects associated with the use of SSAPs, two found negative effects, and twelve found either no benefit or a mix of positive and negative effects. The negative or no association findings were concentrated in studies using IDU community samples that compared users and non-users of SSAPs. In contrast, all eight studies conducted on SSAP clients reported beneficial effects of SSAPs. Five of the six remaining ecological studies, as well as the five modeling studies, also provided findings of beneficial effects of SSAPs. Gibson and associates found that the 14 negative or null studies of sterile syringe access programs were predominately in settings where IDUs can legally purchase low cost syringes at pharmacies, including Canada, the United Kingdom, and the Netherlands. When these studies were excluded, 28 out of the 29 remaining studies demonstrated a protective effect of SSAPs against HIV risk behavior and/or HIV seroconversion.[27]

The New Haven SSAP evaluation was among the first federally funded programs to evaluate the impact of SSAP in the spread of HIV-1 infection among IDUs. The evaluation utilized objective data by tracking and testing exchanged syringes. As a direct result of the New Haven SSAP operations, the mean syringe circulation, or return, time dropped from more than two weeks to less than three days. Through mathematical and statistical modeling, the reduced syringe circulation time was estimated to translate to a 33% reduction in the incidence of HIV infection among the SSAP users.

Opponents of the SSAPs raise several issues associated with SSAPs, such as whether such programs actually promote increasing drug use and crimes in the community. Furthermore, they argue that SSAPs will result in more contaminated syringes on streets and in parks. These issues have been examined by several studies, and their findings have been summarized by Vlahov and Junge,[3] who concluded that SSAPs are not associated with increased drug use and crimes in the community. Since their report in 1998,[3] an additional study was performed to determine whether SSAPs lead to increased drug use among IDUs. Program participants claimed they actually decreased drug use and the sharing of syringes after entering an SSAP.[28] Another study by Broadhead and colleagues[29] concluded that closing an SSAP led to increased drug use among IDUs who had previously used the program. When comparing arrest trends in program and non-program areas before and after the introduction of an SSAP in Baltimore, no significant differences were found. This led to the conclusion that SSAPs do not increase crime in the communities in which they are established.[30] Another study in Baltimore found that two years after an SSAP was opened, there was a significant decrease in the number of publicly discarded needles in the community.[31]

Cost Effectiveness of SSAPs

The CDC has concluded that SSAPs are extremely cost effective. While it takes $190,000 to treat one person diagnosed with HIV, each syringe distributed to IDUs costs less than a dollar.[16] In 2006, federal funds for HIV/AIDS were estimated to total 21.1 billion, of which 58% was for care, 13% for research, 10% for financial compensation and housing assistance, 4% for prevention, and 15% for the international epidemic.[8]

Several government-commissioned committees, as well as, scientific and professional organizations have evaluated the effectiveness of SSAPs such as the National Commission on AIDS, the U.S. General Accounting Office, the Centers for Disease Control and Prevention, as well as, the National Academy of Sciences. Collectively, the findings support the beneficial role of SSAPs with no evidence supporting negative outcomes as a result of SSAPs.[3]

SSAPs as a Form of Harm Reduction

SSAPs are part of a larger public health movement focusing on harm reduction, a strategy for providing aid to those who put their health at risk by engaging in risky behaviors. Based on the harm reduction guidelines established by Jeffrey Kelly, PhD, of the Medical College of Wisconsin's Center for AIDS Intervention Research (CAIR) program, three guidelines direct SSAP harm reduction strategies.[26]

1. **Injection drug users may not be able or willing to change their behavior.**
2. **Public health interventions must work with people in all stages of behavior change.**
3. **Health or social service provider's role should be supportive instead of directive.**

Based on its primary strategy of ensuring that IDUs who cannot or will not stop injecting drugs have legal access to sterile syringes, SSAPs provide sterile syringes for injection drug users at no cost to the individual and establish a way for used syringes to be safely disposed of in an effort to prevent the transmission of HIV, HBV, HCV, and other bloodborne infections. In addition, many SSAPs provide IDUs with a variety of preventive and curative services, such as HIV/AIDS education and counseling, condom and alcohol swab distribution, referrals to substance use treatment, HIV testing, crisis intervention, screening for tuberculosis, HBV, and HCV, and primary medical services.

(Continued on next page)

Sterile Syringe Access Program (SSAP) Established in NJ

SSAPs as a Form of Harm Reduction

(Continued from previous page)

In an effort to reach the maximum amount of IDUs possible, SSAPs may exercise these goals in a range of settings, including storefronts, sidewalk tables, vans, health clinics, and other major locations where IDUs congregate.[2] Today, there are over 185 SSAPs operating in 36 states and Washington DC, Puerto Rico, and Native American lands. New Jersey was the last state in the Northeast to establish an SSAP.[32]

Pharmacies are one of the few sources of sterile syringes other than SSAPs. Some states allow the sale of syringes in pharmacies and it is believed that these sales are part of a comprehensive approach to reduce the risk of transmitting bloodborne pathogens. In 1992, when Connecticut legalized the sale of non-prescription purchase and possession of 10 or fewer syringes, the black market purchase of syringes fell from 74% of the total syringe purchases to 28%. Pharmacies are effective organizations for the sale of syringes because of their convenient store hours, and trained and licensed medical staff. Furthermore, there are no additional expenditures to the government since consumers pay for the syringes and these locations provide privacy for the consumer.[33]

Laws and Opposition

Today, SSAPs face legal and regulatory restrictions, and local community opposition. In addition, the number of IDUs reached by SSAPs is limited. Laws monitoring the sale and distribution of syringes in the United States have their roots in the late 19th and early 20th centuries, when they were created as an effort to inhibit the abuse of opiates, such as morphine. More general drug paraphernalia laws were passed in the 1970s and 1980s in an effort to combat the advertisement, sale, manufacturing, and public possession of drug paraphernalia.[2] Since 1988, federal funding for the distribution of drug paraphernalia for IDUs has been banned.[2] Forty-seven states, Washington, DC and the Virgin Islands have laws that criminalize the sale and possession of drug paraphernalia that is explicitly for drug use. Twenty-three states have pharmacy regulations and requirements that must be met by those who wish to purchase syringes, and eight states and the Virgin Islands require a prescription for syringes. Furthermore, in states that do allow the sale of syringes in pharmacies, some pharmacists are still hesitant to sell them to IDUs.[34] At this time, New Jersey does not allow the sale of syringes in pharmacies.

Researchers at the Center for Drug Use and HIV Research found that opposition to SSAPs takes on a variety of forms, such as institutional opposition (e.g. district attorneys, politicians, and police officers) and community opposition (e.g., opposition organized by clergy and neighborhood associations).[34] Those opposed to SSAPs argue that they encourage drug use, send the wrong message to the country's youth, and increase crime. They also believe that the number of discarded syringes will increase in the communities in which SSAPs are established.

Implementation of Sterile Syringe Access Programs in New Jersey

In 2006, the "Bloodborne Disease Harm Reduction Act" was signed into law in the state of New Jersey. This law established a pilot program to permit a maximum of six municipalities to operate an SSAP. To be eligible to apply to the New Jersey Department of Health and Senior Services (NJDHSS), Division of HIV/AIDS Services (DHAS) for approval to establish an SSAP, the municipality needed to meet certain eligibility criteria. These criteria included: 1) the passage of an ordinance endorsing syringe exchange as a harm reduction strategy that would be implemented to address/reduce the spread of HIV infection; 2) a minimum of 350 people living with HIV/AIDS in the municipality as of December 31, 2006; and 3) a minimum prevalence rate in the municipality attributed to injection drug use of at least 300 per 100,000 population.[1]

DHAS solicited applications from all the eligible municipalities through a Request for Application and a Bidder's/Technical Assistance Conference, and reviewed all applications. As of January 2009, the municipalities approved to establish an SSAP were Atlantic City, Camden, Newark and Paterson.

The SSAPs serve persons 18 years of age or older. The legislatively required minimum programmatic offering for each SSAP as established by the "Bloodborne Disease Harm Reduction Act" is provided on the right. [1]

- The SSAP shall offer information about HIV, HCV, and other bloodborne pathogens and prevention materials at no cost to consumers.
- The SSAP shall seek to educate all consumers about the safe and proper way to dispose of needles and syringes.
- The SSAP shall provide information and referrals for drug treatment and encourage that each consumer receives an HIV test and develop an individualized drug use treatment plan.
- The SSAP shall provide information and referrals for available health and social service options relevant to the consumer's needs.
- The SSAP shall maintain confidentiality by using confidential identifiers.
- The SSAP shall provide a uniform identification card to consumers, staff, and volunteers involved in transporting, exchanging, or possessing syringes and needles.
- The SSAP shall provide consumers with a schedule of program operation hours and locations, and shall provide information about prevention and harm reduction strategies and drug abuse treatment services when they enroll in the SSAP.
- The SSAP shall dispose of the needles and syringes properly and develop and maintain protocols for post-exposure treatment.

Evaluation & Assessment of SSAPs in New Jersey

In order to assess the public health effectiveness of the New Jersey Sterile Syringe Access Demonstration Program (NJSSADP), the New Jersey Legislature requires a thorough evaluation of the program. The University of Medicine and Dentistry of New Jersey-School of Public Health (UMDNJ-SPH) is utilizing the following specific objectives to collect and analyze the data necessary to do a formative program evaluation.[1]

- To determine the number of consumers participating in the NJSSADP and access their reasons for participating in the programs.
- To determine the number of exchanged syringes and needles and evaluate the disposal of syringes and needles that are not returned by consumers.
- To determine the number of consumers in the NJSSADPs who participated in drug abuse treatment programs.
- To assess whether an adequate number of drug treatment program slots is available to meet the treatment needs of persons who have been referred to drug abuse treatment programs by the NJSSADPs.
- To determine the number of consumers in the NJSSADPs who benefited from counseling and referral to programs and entities that are relevant to their health, housing, social service, employment, and other needs.
- To determine if there is any increase or decrease in the spread of HIV, HCV, and other bloodborne pathogens that may be transmitted by the use of contaminated syringes and needles.
- To consult with local law enforcement authorities regarding the impact of NJSSADP on the rate and volume of crime in the affected municipalities.
- To obtain data from public safety and emergency medical service providers statewide regarding the incidence and location of needle stick injuries to their personnel.
- To determine the impact of NJSSADPs on drug use and high-risk sexual practices.
- To monitor the community image of NJSSADPs and identify unanticipated effects NJSSADPs on the community.

In accord with the Bloodborne Disease Harm Reduction Act, "the Commissioner of Health and Senior Services shall report to the Governor and the Legislature, no later than one year after the effective date of this act and biannually thereafter, on the status of sterile syringe access programs established pursuant to" the law.[1] The New Jersey Department of Health and Senior Services issued a report in January 2009 to the Legislature and the Governor's Advisory Council on HIV/AIDS and Related Bloodborne Pathogens, detailing the first-year results of New Jersey's needle-exchange effort. This report incorporates the data obtained and analyzed by the UMDNJ-School of Public Health from the four SSAPs operating in New Jersey, in Atlantic City, Camden, Paterson, and Newark.[35]

Atlantic City – The Atlantic City SSAP was opened on November 27, 2007 and in the first 13 months the program had **576 program participants,** distributed 60,001 needles and received 31,787 in returned needs, an exchange rate of 52.9%. This site was developed as a collaboration between the Atlantic City Health Department and the South Jersey AIDS Alliance (SJAA). The project has had extensive media coverage for several years, and coverage since the site opened has been positive, highlighting the active support of the Director of Atlantic City Health and Human Services. The SSAP site is on the second floor of OASIS, a community center run by SSJA, which is well established as a local resource. The center is located directly across the street from a drug treatment center, which allows for easy treatment referrals. Thirteen percent of participants accepted drug treatment referrals in the first year. All program participants are provided with an identification card that verifies their status as clients of the local NJSSADP.

Camden – Camden's SSAP opened on January 15, 2008. In its first year, it had approximately **514 program participants**. They distributed 38,798 needles and 6,226 were returned, an exchange rate of 16%. This site has been able to refer 56.4% of participants to drug treatment. This site is run by the Camden Area Health Education Center (AHEC) from a mobile van, targeting an area of high drug use in South Camden. The Camden SSAP is planning to extend the hours of operation and plan to open another mobile site in the near future.

Paterson – The Paterson SSAP opened on January 30, 2008 and in the first 11 months, had **421 participants,** and dispensed 22,890 needles, of which 54.3% (174) were returned. The program, run by the Paterson Counseling Center, is housed at the Well of Hope Drop-In Center, which is known throughout the community and has an established clientele, facilitating the recruitment of participants into the SSAP.

The Paterson SSAP has referred 41.3% of its participants to drug treatment program. Treatment options include the Paterson Counseling Center and the mobile van, a recent addition that allows participants to receive treatment without being confined to a treatment center. The SSAP has been successful in garnering positive media attention about the extent of intravenous drug use, the need for syringe exchange, and the new program.

Newark – The SSAP in Newark opened on February 19, 2008. In its first four months, it served **297 participants,** to whom it dispensed 14,822 needles, of which 40.4% percent were returned. The site has referred 34.3% of participants to drug treatment. They have had a rapid response to its recruitment efforts, focused on areas with high rates of IDU in the city of Newark. This site is operated by the North Jersey Community Research Initiative (NJCRI), is housed in their building and staffed by two NJCRI employees.

In the first year following legalization, the four Sterile Syringe Access Programs have been very successful: they have **served a total of 1,808 injecting drug users (IDUs),** and dispensed 141,368 needles, of which 43.5% (61,495) were returned. The programs also offered referrals to drug treatment programs, and 640 people, or 35.4% of participants, requested and received these referrals.[35]

Conclusion

Access to clean syringes and needles is vital in reducing the risk of transmission of bloodborne pathogens including HIV, hepatitis B and hepatitis C. The establishment of a demonstration sterile syringe access program in four New Jersey cities is encouraging, although it has only reached a small proportion of IDUs to date. Several steps have been identified to further reduce the harm of injection drug use and provide more legal access to clean syringes. Legislation allowing the purchase of syringes from pharmacies, allowing physicians to prescribe syringes to IDUs, and expansion of the SSAP to other large New Jersey cities would also provide health benefits to both IDUs and their communities.

REFERENCES

1. Bloodborne Disease Harm Reduction Act. State of New Jersey – 212th Legislature. October 20, 2006.
2. Centers for Disease Control and Prevention. Update: Syringe Exchange Programs: January 2002. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5427a1.htm. Accessed January 2, 2009.
3. Vlahov D, Junge B. The Role of Needle Exchange Programs in HIV Prevention. *Public Health Rep.* 1998:13 (suppl 1):75-80.
4. New Jersey Department of Health and Senior Services, Public Health Services Branch, Division of HIV/AIDS Services. Preventing Disease with Care. Profile of the State of New Jersey, 2005.
5. Centers for Disease Control and Prevention. HIV Diagnoses among Injection Drug Users in States with HIV Surveillance – 25 states, 1994-2000. *MMWR.* 2003:2(27):634-636.
6. Hall IH, Lee LM, Li J, Song R, McKenna MT. Describing the HIV/AIDS Epidemic: Using HIV Case Data in Addition to AIDS Case Reporting. *Ann Epidemiol.* 2005:5(1):5-12.
7. State of New Jersey Department of Health and Senior Services. New Jersey HIV/AIDS Report: June 30, 2008. http://www.state.nj.us/health/aids/documents/qtr608.pdf Accessed December 30, 2008.
8. Centers for Disease Control and Prevention. Basic Information. http://www.cdc.gov/hiv/topics/basic/index.htm. Accessed June 7, 2008.
9. Hall HI, Song R, Rhodes P, et al, for the HIV Incidence Surveillance Group. Estimation of HIV Incidence in the United States. *JAMA,* August 6, 2008:300(5):520.
10. Centers for Disease Control and Prevention. A Glance at the HIV/AIDS Epidemic. http://www.cdc.gov/hiv. Accessed June 7, 2008.
11. Henry J. Kaiser Family Foundation. The HIV/AIDS Epidemic in the United States: March 2008. http://www.kff.org/hivaids/upload/3029-08.pdf. Accessed December 30, 2008.
12. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report: Cases of HIV Infection and AIDS in the United States and Dependent Areas, 2006. http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2006report/ Accessed December 30, 2008.
13. Centers for Disease Control and Prevention. Hepatitis B. http://www.cdc.gov/hepatitis/HBV.htm. Accessed December 30, 2008.
14. Centers for Disease Control and Prevention. Viral hepatitis C. www.cdc.gov/hepatitis/HCV.htm. Accessed December 30, 2008.
15. Drug Policy Alliance Network. Campaign for a Healthier New Jersey Syringe Access. http://www.drugpolicy.org/about/stateoffices/newjersey/chnj. Accessed June 7, 2008.
16. State of New Jersey Department of Health and Senior Services. Communicable Disease Service Statistics. http://www.state.nj.us/health/cd/stats.htm. Accessed June 8, 2008.
17. State of New Jersey Department of Health and Senior Services. New Jersey Strategic Plan for Hepatitis C Prevention and Control: January 2005. http://www.state.nj.us/health/cd/documents/hepatitisc_strategic_plan.pdf. Accessed June 8, 2008.
18. Gertel-Rosenberg A, Hailu Y. Estimating the Extent of Illicit Drug Abuse in New Jersey Using Capture-Recapture Analysis. Division of Addiction Services, New Jersey Department of Human Services, July 2005.
19. Substance Abuse and Mental Health Services Administration's Office of Applied Studies. National Survey on Drug Use and Health: 2002, 2003, and 2004.
20. Centers for Disease Control. Trends in Injection Drug Use Among Persons Entering Addiction Treatment – New Jersey, 1992-1999. *MMWR* Morb Mortal Wkly Rep. 2001:0(19):378-381.
21. Weinbaum CM, Sabin KM, Santibanez SS. Hepatitis B, hepatitis C, and HIV in Correctional Populations: A Review of Epidemiology and Prevention. *AIDS.* 2005:19(suppl 3):S41-S46.
22. Johnston LD, O'Malley PM. The Recanting of Earlier Reported Drug Use by Young Adults. *NIDA Res Monogr.* 1997: 167:59-80.
23. Armstrong GL. Injection Drug Users in the United States, 1979-2002: An Aging Population. *Arch Intern Med.* 2007:167(2):166-173.
24. Jacobs R, Toynton P. Syringe Exchange. *N J Med.* 2003:100(9 suppl):55-59.
25. Hagan H, Jarlais DC, Friedman SR, Purchase D, Alter MJ. Reduced Risk of hepatitis B and hepatitis C Among Injection Drug Users in the Tacoma Syringe Exchange Program. *Am J Public Health.* 1995:85(11):1531-1537.
26. Wright NM, Tomkins CN. A Review of the Evidence for the Effectiveness of Primary Prevention Interventions for hepatitis C Among Injecting Drug Users. *Harm Reduct J.* 2006:27-35.
27. Gibson DR, Flynn NM, Perales D. Effectiveness of Syringe Exchange Programs in Reducing HIV Risk Behavior and HIV Seroconversion among Injecting Drug Users. *AIDS.* 2001:5(11):1329-1341.
28. Valente TW, Vlahov D. Selective Risk Taking among Needle Exchange Participants: Implications for Supplemental Interventions. *Am J Public Health.* 2001:91(3):406-411.
29. Broadhead RS, Van Hulst Y, Heckathorn DD. The Impact of a Needle Exchange's Closure. *Public Health Rep.* 1999:114(5):439-447.
30. Marx MA, Crape B, Brookmeyer RS., et al. Trends in Crime and the Introduction of a Needle Exchange Program. *Am J Public Health.* 2000:0(12):1933-1936.
31. Doherty MC, Junge B, Rathouz P, Garfein RS, Riley E, Vlahov D. The Effect of a Needle Exchange Program on Numbers of Discarded Needles: A Two-Year Follow-Up. *Am J Public Health.* 2000:90(6):936-939.
32. Bluthenthal RN, Heinzerling KG, Anderson R, Flynn NM, Kral AH. Approval of Syringe Exchange Programs in California: Results from a Local Approach to HIV Prevention. *Am J Public Health.* 2008: 98(2):278-283.
33. Centers for Disease Control and Prevention. Pharmacy Sales of Sterile Syringes: December 2005. http://www.cdc.gov/IDU/facts/AED_IDU_PHAR.pdf. Accessed June 7, 2008.
34. Tempalski B, Flom PL, Friedman SR, et al. Social and Political Factors Predicting the Presence of Syringe Exchange Programs in 96 US Metropolitan Areas. *Am J Public Health.* 2007:97(3):437-447.
35. Clark M. Atlantic City needle exchange produces mixed results . Press of Atlantic City. January 19, 2009; News. Retrieved January 20, 2009 from http://www.pressofatlanticcity.com/180/story/377084.html.

Sterile Syringe Access Programs (SSAPs) in New Jersey

Atlantic City SSAP
Atlantic City Health Department
and South Jersey AIDS Alliance
Site: OASIS Drop-In center
32 S. Tennessee Ave., Atlantic City
(609) 572-1929
Tuesdays and Thursdays,
10 AM to 2 PM

Paterson SSAP
Paterson Counseling Center
and Well of Hope
Site: Well of Hope Drop-In Center
207-209 Broadway, Paterson
(973) 523-0700 x10
Monday, Wednesday, Friday
10 AM to 2 PM

Newark SSAP
NJCRI (North Jersey Community
Research Initiative)
Access Program
Site: 393 Central Ave. at 1st St., Newark
(enter through parking lot)
(973) 483-3444, x202 or 134
Monday and Tuesday, 1 PM to 4 PM;
Wednesday, Thursday, and Friday,
10 AM to 1 PM

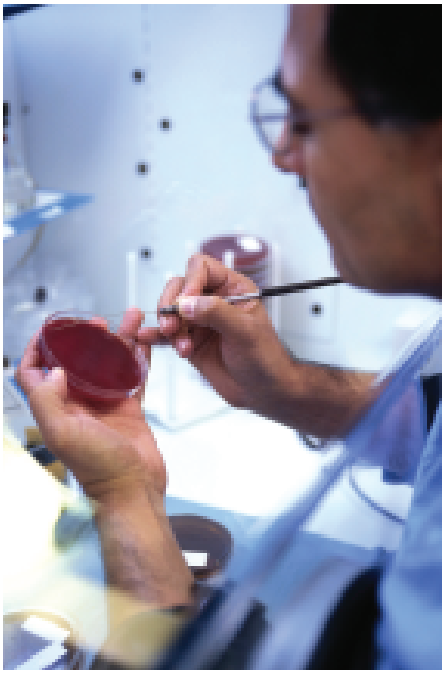
Camden SSAP
Camden Area Health Education
Center (AHEC)
Lifeworks Program
Site: Mobile van
(856) 963-2432 x220
Tuesday, 1:30 PM to 4:30 PM

New HIV Type 2 Subvirus Identified in Newark

Stephen Smith, MD, of the Peter Ho Clinic, Infectious Disease, at St. Michael's Medical Center in Newark, NJ, with researchers at the Tulane National Primate Research Center and Department of Tropical Medicine, School of Public Health, Tulane University, isolated a new virus from the blood of a man from Sierra Leone. HIV type 2 is less common and less aggressive than HIV type 1. However, this new virus, which is essentially a monkey virus, appears to be more pathogenic than other strains of HIV type 2. It was named according to the current nomenclature, HIV2NWK08F (the "NWK" stands for Newark, the "08" stands for the year 2008 and "F" stands for the virus subtype).

HIV2NWK08F is much different than any virus seen in humans before. Although the risk is small, this new virus could theoretically spread and cause a outbreak of HIV-2 infection. Without this publication, such an outbreak would have gone undetected, since the virus is so divergent. Now, health authorities in Sierra Leone and elsewhere have been alerted that a subtype of HIV-2, which is not detected by PCR for epidemic HIV-2 strains, exists and can lead to immunosuppression.

http://www.retrovirology.com



Guidelines Update

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 November 3, 2008.

http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf

THIS UPDATED SET OF HIV TREATMENT GUIDELINES INCLUDES THE FOLLOWING REVISIONS OR NEW FEATURES:

Laboratory monitoring

- A new table (Laboratory Monitoring Table 3) provides recommendations for laboratory test results to obtain at baseline, and while receiving antiretroviral therapy, to monitor for safety and treatment responses.
- Resistance testing should be considered in patients with viral loads 500 to 1000 copies/mL, resistance testing, although it may not always be reliable at these levels.

Treatment for antiretroviral-naive patients

For protease inhibitor–based regimens:

- Ritonavir-boosted darunavir has been added as a preferred protease inhibitor component.
- Except for pregnant women, once-daily ritonavir-boosted lopinavir has been moved from an alternative to a preferred protease inhibitor component.

For dual-nucleoside reverse transcriptase inhibitor (NRTI) options:

- Abacavir plus lamivudine has been moved from a preferred to an alternative dual-NRTI component. This decision results from large observational cohort studies suggesting an increased risk for myocardial infarction in patients with high cardiac risk factors, and concerns regarding virologic potency in patients with baseline viral loads 100,000 copies/mL.

Combinations no longer indicated or that should be used only with caution:

- The combination of unboosted atazanavir plus didanosine plus emtricitabine (or lamivudine) is not recommended because of efficacy concerns.
- The combination of nevirapine plus tenofovir plus emtricitabine (or lamivudine) should be used only with caution and with close monitoring of virologic responses, because several small studies suggested early virologic failure.

Management of Treatment-Experienced Patients

For treatment-experienced patients, a new section summarizes recommendations for regimen simplification.

Summarized from:

Panel on Antiretroviral Guidelines for Adults and Adolescents.
Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.
Department of Health and Human Services. November 3, 2008; 1-139.
Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf,
Accessed December 11, 2008.

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

AIDS InfoNet
New Mexico AIDS Education and Training Center-sponsored site provides frequently updated fact sheets on HIV/AIDS services and treatments in both English and Spanish www.aidsinfonet.org

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:

- Role of Newly Approved HIV Antiretroviral Agents in Treatment-Experienced Patients
- Medical Implications of Injection Drug Use
- Perinatal HIV Prevention and the 2007 New Jersey Legislation
- Metabolic Complications Associated with the Treatment of HIV-Infected Persons

NEW JERSEY January 2009
AIDS Line

PUBLISHED BY

UNIVERSITY OF MEDICINE & DENTISTRY OF NEW JERSEY

Center for Continuing & Outreach Education
Division of AIDS Education

with

New Jersey Department of Health and Senior Services, Division of HIV/AIDS Services

UMDNJ-CCOE-AIDS
30 Bergen Street, ADMC 710
PO Box 1709, Newark, NJ 07101-1709
Tel: 973-972-3690 • Fax: 973-972-3371
www.umdnj.edu/ccoe/aids

SAVE THE DATE

THURSDAY, JUNE 11, 2009

HIV Clinical Update

Sheraton at Woodbridge Place
515 Route One South • Iselin, New Jersey

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

FOR MORE INFORMATION ON ALL CONFERENCES:
http://ccoe.umdnj.edu/catalog/aids or call the UMDNJ-Center for Continuing & Outreach Education, Division of AIDS Education: (973) 972-3690

NEW JERSEY January 2009 AIDS Line **MAILING LIST**

Please print.
This form may be photocopied.

To update your free subscription to *NJ AIDSLine,* please complete this form and fax to us with your mailing label. If this issue wasn't mailed to you, please complete the form and check "new." **Fax to: (973) 972-3371**

- ☐ **NEW:** Please add me to your list.
- ☐ **UPDATE my listing:** Must include label; note changes on label or form.
- ☐ **STOP:** Please take me off the list. (include label section, or write name & address)

Name:
Address:
City:
State: Zip:
E-mail address: Fax:

UMDNJ University of Medicine & Dentistry of New Jersey

CENTER FOR CONTINUING & OUTREACH EDUCATION
DIVISION OF AIDS EDUCATION
30 Bergen Street, ADMC 7, P.O. Box 1709
Newark, New Jersey 07101-1709

Non-Profit Organization
U.S. Postage
PAID
UMDNJ