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*New Jersey*

**AIDSLINE**

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*Director's Message*

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In its 2003 report on *Health Professions Education: A Bridge to Quality*, the Institute of Medicine's Board on Healthcare Services recognized that a commitment to lifelong learning is one of the important competencies that clinicians require in patient care in the 21st century. This report recognized that simply asking healthcare professionals to do more would not solve any quality of care issues. *Medical Meetings* magazine, in its 15th Annual Physician Survey (October 2004) found that physicians actually spent less time participating in CME activities in 2004 versus 2003, citing time pressure as the primary reason (*Medical Meetings*, January 2005). In the same issue, they reported continued growth in distance learning education, including print and online CME. Today's media saturated environment surrounds the healthcare professional with an overwhelming array of information. Providing formal CE credit raises the bar, and helps the healthcare professional choose from among the milieu. As a clinician working to combat a virus that evolves faster than our multi billion-

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Our goal for *New Jersey AIDSLine* is to make it one of the tools at your disposal to help you manage the information you need to stay current in HIV/AIDS. We look forward to your comments and suggestions. Please contact me at [richetdi@umdnl.edu](mailto:richetdi@umdnl.edu) with any ideas or thoughts you have on *New Jersey AIDSLine*.

Dion A. Richetti, DC  
Director

**SAVE THE DATE!**  
HIV Clinical Update 2005:  
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Thursday June 16, 2005  
Iselin, New Jersey  
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## RAPID DIAGNOSTIC TESTING FOR HIV: CLINICAL IMPLICATIONS OF A NEW DIAGNOSTIC TOOL

### TARGET AUDIENCE:

This activity is designed for physicians and nurses.

### STATEMENT OF NEED:

The CDC recommended incorporation of Rapid HIV testing in both HIV prevention programs and regular primary care, as an important tool to improve earlier identification of individuals with HIV infection and to engage them in HIV medical care (HIV Prevention: New Strategies for a Changing Epidemic, April 2003). The CDC also published guidelines for use of rapid testing to reduce vertical transmission when women present in labor with unknown HIV status.

New Jersey Department of Health and Senior Services (NJDHSS) data indicates that the post-test counseling rate at publicly funded counseling and testing sites has improved from 65% to 99% in the 10,601 tests conducted in the first year of rapid HIV testing, beginning in November 2003. The proportion of persons testing HIV positive increased from 2% to 2.5% with rapid HIV testing, and 59% were newly identified. These people are referred for treatment, prevention services, and social services. Clinicians who are aware of benefits, availability, and strategies for incorporating Rapid HIV testing in their practices will be more likely to use it as a tool to increase early detection and treatment of HIV infection and AIDS.

### LEARNING OBJECTIVES:

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

- Recognize the clinical diagnostic role of rapid HIV testing.
- Understand the role of rapid HIV testing to reduce the risk of vertical transmission when women present in labor with unknown HIV status.
- Assess if rapid HIV testing can be integrated into their practice setting.
- Define when preliminary positive rapid test results can be used to start antiretroviral therapy.
- Discuss confirmatory HIV testing for preliminary positive rapid test results.

### 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 consisting 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 CME credit letter awarding AMA/PRA category 1 credit and the test answer key six (6) weeks after receipt of the self-assessment test, registration, and evaluation materials.

Estimated time to complete this activity as designed is 1 hour.

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 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

The activity was prepared in accordance with the ACCME Essentials.

This activity was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Dion Richetti, DC, Patricia Kloser, MD, MPH, and Bonnie Abedini, BSN, RN.

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### DISCLOSURE:

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, all program faculty are required to disclose to the activity participants:

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### FACULTY DISCLOSURE DECLARATIONS:

The faculty listed below declare that they have no financial relationships with any corporate organization whose product(s) will be discussed in this presentation:

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### DISCLAIMER:

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The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult the full prescribing information on any agent(s) presented in this activity for recommended dosage, indications, contraindications, warnings, precautions, and adverse effects before prescribing any medication. This is particularly important when a drug is new or infrequently prescribed.

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### GRANTOR ACKNOWLEDGEMENT

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# Rapid Diagnostic Testing for HIV: Clinical Implications of a New Diagnostic Tool

CME

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## Learning Objectives

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

1. Recognize the clinical diagnostic role of rapid HIV testing.
2. Understand the role of rapid HIV testing to reduce the risk of vertical transmission when women present in labor with unknown HIV status.
3. Assess if rapid HIV testing can be integrated into their practice setting.
4. Define when preliminary positive rapid test results can be used to start antiretroviral therapy.
5. Discuss confirmatory HIV testing for preliminary positive rapid test results.

## ABSTRACT

Over the past ten years there have been numerous advances in HIV counseling, testing, and referral practices. One of the most recent advances in the diagnosis of HIV disease is the introduction of rapid HIV testing that can be incorporated into daily practice to:

- 1) assist in diagnosis and counseling of patients with HIV disease,
- 2) reduce the risk of vertical HIV transmission for women who present in labor with unknown HIV status,
- 3) as part of the initial evaluation of a patient for non-occupational postexposure prophylaxis, and
- 4) decrease the risk of occupational HIV transmission.

Rapid HIV testing can be accomplished at the point-of-care in as little as 10 to 20 minutes or may be done in a laboratory. As a result, strategies and practices regarding testing and counseling need to be revisited, particularly when rapid HIV results can make a crucial difference in counseling and initiating effective treatment.

## INTRODUCTION

The worldwide HIV pandemic has been devastating. Through the end of 2003 an estimated 40 million people were living with HIV/AIDS. Approximately 14,000 people are thought to be infected daily; over 5 million people became infected and nearly 3 million died of AIDS in 2003.<sup>1,2</sup> In the United States between 850,000 and 900,000 individuals are living with HIV, including 180,000 to 280,000 who do not know that they are infected. An estimated 40,000 new infections occur each year.<sup>3,4</sup>

New Jersey is a high prevalence state, ranking 5th in the United States in cumulative reported AIDS cases, third in cumulative reported pediatric AIDS cases, and having the largest proportion of women among its cumulative reported AIDS cases.<sup>2</sup> At mid-2004, 32,401 people were living with HIV or AIDS in New Jersey.<sup>5</sup>

### SECTION I: RAPID DIAGNOSTIC TESTING FOR HIV: CLINICAL IMPLICATIONS

HIV counseling and testing needs to be integrated into the routine medical care of patients.<sup>6</sup> Clinicians frequently have patients to whom HIV testing should be offered. These include:

- Pregnant women,
- Persons with a possible acute occupational exposure,
- Patients with a known sexual or needle-sharing exposure to the virus,
- Patients in settings serving populations at increased behavioral or clinical risk,
- Patients in areas in which the prevalence of HIV disease is 1% or greater,
- Patients with a self-reported HIV risk behavior, such as injection drug use, men who have sex with men, and unprotected vaginal or anal intercourse with more than one sexual partner or with a partner who may be infected with HIV,
- Patients who specifically request an HIV test,
- Patients with clinical signs or symptoms of HIV disease (e.g., fever, illness of unknown origin, oral thrush, unexplained lymphadenopathy with or without weight loss, psoriasis, or laboratory values suggestive of HIV disease, e.g., low white blood count, anemia), and
- Patients with a diagnosis suggesting increased risk of HIV disease such as opportunistic infections, tuberculosis, cervical or anal cancer, Kaposi's sarcoma, lymphoma, recurrent pneumonia or bacteremia, hepatitis B, hepatitis C, or a sexually transmitted disease should be offered counseling and testing.<sup>7,8</sup>

The major focus of HIV prevention and control has been to promote the acceptance of risk reducing behaviors through prevention counseling and testing and to facilitate linkage to medical prevention and other support services.<sup>6</sup> Testing has played a major role in reducing the transmission of HIV. The percentage of adults in the United States who obtain an HIV test has remained 10 – 12% per year for more than a decade.<sup>9</sup>

Early and rapid diagnosis of HIV began to assume particular importance as effective combination antiretroviral therapy became available. Combination therapy contributes to reducing the risk of vertical and occupational HIV transmission while improving the quality of life and the longevity of persons infected with HIV disease. A significant reduction in the lag time between risk exposure and the availability of testing results required the evolution of a new approach to HIV testing – the rapid HIV test. Six rapid HIV tests have been approved by the United States Food and Drug Administration (FDA) for commercial use: the Single Use Diagnostic System for HIV-1, (SUDS, Abbott Laboratories, Abbott Park, IL—no longer marketed), OraQuick® HIV1 and the OraQuick® Advance HIV-1/HIV-2, (OraSure Technologies, Bethlehem, PA), Reveal™ G2 Rapid HIV-1 Antibody Test (MedMira Laboratories, Halifax, Nova Scotia), Uni-Gold™ Recombigen® HIV (Trinity Biotech plc, Wicklow, Ireland), and Multispot HIV-1/HIV-2 (Bio-Rad Laboratories, Hercules, CA). Additional rapid HIV tests are under consideration by the FDA.

Because rapid point-of-care testing offers 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.<sup>6</sup> Rapid HIV testing offers the advantage of providing test results at the time of the behavioral intervention.

Rapid diagnostic HIV testing has several clinical applications. This paper describes rapid HIV testing and its role in:

- 1) reducing vertical HIV transmission for women who present in labor with unknown HIV status,
- 2) reducing the risk of occupational transmission of HIV,
- 3) as part of the initial evaluation of a patient for non-occupational postexposure prophylaxis, and
- 4) assisting in diagnosis and counseling of patients with HIV disease.

Rapid HIV testing plays a crucial role in time-sensitive decisions regarding the need for prophylaxis to reduce transmission in cases of occupational exposures and women presenting in labor with unknown HIV status.<sup>10</sup> Detailed information on these rapid HIV tests, their interpretation, counseling, and laboratory licensure

requirements is provided in the second section of this article: *“Rapid Testing: A New Diagnostic Tool for HIV.”*

### **DIAGNOSIS OF PATIENTS USING RAPID HIV DIAGNOSTIC TESTING**

The CDC currently recommends that all providers integrate HIV counseling and testing into routine practice.<sup>6</sup> 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. A major issue in the United States has been patients who present for HIV counseling and testing and who do not return to receive their test results and posttest counseling. The Centers for Disease Control and Prevention (CDC) reported that of 2.5 million persons tested in 1995, 25% of those testing positive and 33% of those testing negative did not receive their test results. CDC calculated that a total of 697,495 more persons nationwide would have learned their HIV status if rapid HIV testing was used.<sup>11</sup>

Integration of rapid HIV testing in daily practice can allow prompt diagnosis of patients with HIV disease. These patients can then be referred to a provider with experience and expertise treating HIV patients. In addition, these patients can be referred for prevention and social services.

### **RAPID TESTING AT PUBLICLY FUNDED COUNSELING AND TESTING SITES IN NEW JERSEY**

Rapid HIV testing, using OraQuick®, has been available at publicly funded HIV counseling and testing sites in New Jersey since November 2003. It is currently offered at 51 sites with expansion to approximately 200 sites anticipated to occur by the end of 2005.

Through the first year of rapid HIV testing, 10,601 tests were performed with 10,469 (99%) of persons receiving results. Most persons (10,329, 97.4%) tested negative and 268 (2.5%) tested positive. Of those testing positive, 159 (59.3%) represent newly identified persons with HIV disease. Four persons (0.04%) had discordant results in which the rapid HIV test was positive and the confirmatory Western blot was negative.

Remarkable improvement has been noted in the percentage of persons receiving test results (65% prior to rapid HIV testing and 99% with rapid HIV testing) and in the proportion of persons tested who are HIV positive (2% prior to rapid HIV testing and 2.5% with rapid HIV testing). In addition almost two-thirds of the persons testing positive for HIV are newly identified. These people are referred for treatment, prevention services, and social services.

### **RECOMMENDATIONS FOR RAPID HIV TESTING OF WOMEN IN LABOR**

Prevention of vertical HIV transmission has been an important success story in the HIV pandemic. The risk of transmission has been reduced from approximately 25% to less than 2% by using currently recommended obstetrical interventions and prenatal combination antiretroviral therapy in women aware of their HIV infection early in pregnancy.<sup>10</sup> In New Jersey, the perinatal transmission rate has decreased from 21% in 1991 to less than 4% in 2004.<sup>5</sup>

In New Jersey, regulations require that all pregnant women receive counseling and be offered a voluntary HIV test.<sup>12</sup> Ideally all pregnant women should be offered HIV testing during an initial prenatal visit, to allow for timely initiation of treatment to reduce the chance of vertical transmission. However, a particular area of concern is women who present in labor with unknown HIV status (HIV test results not documented on the medical record). These women may not have been offered HIV counseling and testing during pregnancy, may have opted not to have an HIV test during pregnancy, or may not have received prenatal care. Clinical trial data have shown that antiretroviral medications, even when started during labor and delivery and continued in the neonatal period, can reduce mother-to-child HIV transmission by up to fifty percent.<sup>13-15</sup>

When women present in labor with unknown HIV status, the key to maximal perinatal HIV risk reduction is rapid HIV testing and initiation of short course therapy. The CDC sponsored Mother-Infant Rapid Intervention at Delivery (MIRIAD) study showed that offering voluntary HIV testing during labor is feasible in obstetrical settings. In addition, point-of-care testing has been shown to provide results faster than sending specimens to the hospital laboratory for rapid HIV testing.<sup>16</sup> The CDC recommends rapid HIV testing for women in labor whose HIV status is unknown.<sup>17</sup>

The NJDHSS has established a standard of care in which women who present in labor with unknown HIV status should receive counseling and be offered voluntary rapid HIV testing. If a preliminary positive rapid HIV test result is obtained, women can be offered a short course therapy with referral to a physician with experience and expertise treating HIV disease for both the mother and the child.<sup>12</sup> The *“Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States - June 23, 2004”* describes four options for short course therapy.<sup>13</sup>

## **RECOMMENDATIONS FOR RAPID HIV TESTING FOLLOWING POTENTIAL OCCUPATIONAL HIV EXPOSURE**

Transmission of blood-borne pathogens is an occupational hazard for health care workers. The average risk of HIV infection from all types of percutaneous exposures to HIV-infected blood is approximately 0.3 percent. A CDC case control study showed that the risk of HIV-infection exceeded 0.3 percent for exposures that involved a deep injury to the health care worker; visible blood on the device that caused the injury; a device that had been placed in the source patient's vascular system, (e.g., a needle used for phlebotomy); or a source-patient who died as a result of AIDS within 60 days post-exposure.<sup>18</sup>

The average risk of HIV infection following a mucous membrane or skin exposure is less than the risk associated with a percutaneous exposure. After a mucous membrane exposure the average risk of HIV infection is 0.09 percent. The average risk of HIV infection after a skin exposure is less than 0.09 percent. The risk for skin exposure may be increased if skin contact is prolonged, if contact involved an extensive area of the skin, if the integrity of the skin is not intact, or if the exposure involves a higher titer of HIV.<sup>18</sup>

Following a high-risk occupational exposure, employers need to provide health care workers with a system for prompt evaluation, counseling, and follow-up. First aid needs to be administered immediately after an exposure. Puncture wounds and other cut injuries should be washed with soap and water. If oral and/or nasal mucosa has been exposed, they should be decontaminated by flushing with water. Eyes should be irrigated with clean water and saline or sterile irrigants that are designed for flushing eyes. The exposure should be reported to the person or department (e.g., employee health, infection control) responsible for managing exposures.<sup>19</sup>

The key to reducing the risk of occupational HIV transmission is to provide post-exposure prophylaxis as soon as possible following a potential exposure. Testing to determine the HIV status of the source of the exposure should be conducted as soon as possible after the incident. The exposure source should receive pre and post-test counseling and give consent for HIV testing. A rapid HIV-antibody test kit approved for use in the jurisdiction should be considered particularly if testing by EIA cannot be completed in 24-48 hours. Positive results by EIA or rapid HIV-antibody tests are considered to be highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody. Confirmation of a reactive result by Western blot or IFA is not necessary to make initial decisions regarding post-exposure management but they should be completed before informing the source person.<sup>18,19</sup>

HIV antibody tests should be performed on the exposed employee immediately to establish a baseline and then periodically for at least six months post-exposure, e.g., 6 weeks, 12 weeks, and six months. HIV testing should be performed on any health care worker who has an illness compatible with an acute retroviral syndrome following an occupational exposure, regardless of the interval since the exposure. HIV antibody testing using enzyme immunoassay (EIA) should also be used to monitor for HIV seroconversion. The routine use of direct assays, e.g., HIV antigen EIA or polymerase chain reaction for HIV RNA, to detect infection in health care workers is generally not recommended. The reliability of HIV RNA testing to detect very early infection has not been determined and it is not FDA approved for this purpose. The employee should be counseled on precautions to prevent secondary transmission of HIV.<sup>18</sup>

If appropriate, CDC recommendations for post-exposure prophylaxis (PEP) with laboratory monitoring should be offered to the employee. Although animal studies suggest that PEP probably is substantially less effective when started more than 24-36 hours post-exposure, the interval after which no benefit is gained from PEP for humans is undefined. In humans, the interval within which PEP should be initiated for optimal efficacy is not known. Therefore, if appropriate for the exposure, PEP should be started even when the interval since exposure exceeds 36 hours. Initiating therapy after a longer interval (e.g., one-week) might be considered for exposures that represent an increased risk for transmission.<sup>20</sup>

## **RECOMMENDATIONS FOR RAPID HIV TESTING FOLLOWING POTENTIAL NONOCCUPATIONAL HIV EXPOSURE**

Because persons who are infected with HIV might not be aware they are infected, baseline HIV testing should be performed on all persons seeking evaluation for potential nonoccupational HIV exposure. If possible, this should be done with an FDA-approved rapid test kit (with results available within an hour). If rapid tests are not available, an initial treatment decision should be made based on the assumption that the potentially exposed patient is not infected, pending HIV test results.<sup>21</sup>

## **SECTION II: RAPID HIV TESTING: A NEW DIAGNOSTIC TOOL FOR HIV DETECTION**

Antibody testing to diagnose HIV was introduced in 1985.<sup>8</sup> At that time, most testing was performed in large laboratories equipped with highly trained technologists who performed testing in batch assays. Such an approach allowed facilities to develop effective labor-saving quality control techniques while insuring the reliable performance of tests, but it also led to infrequent testing and long turn-around-times. The standard

laboratory HIV testing protocol involved multiple steps with varying delays at each step along the way:

1. Specimen procurement via phlebotomy.
2. Transportation to a central laboratory.
3. Assay specimens utilizing EIA or IFA.
4. Enzyme Immunoassay screening procedure performed by trained medical technologists.
  - If POSITIVE: Repeat, then perform a confirmatory test (Western Blot or IFA) if repeatedly reactive.
  - If NEGATIVE: Generate a report.
5. Report generation and review by the laboratory director.
6. Transmittal to the patient's physician or HIV counselor.
7. Result review with the patient.

From a technical perspective these procedures were very sensitive and quite specific.

The lag time between obtaining a specimen and providing results is a time of high anxiety and significant stress for many patients. While the time to perform an HIV antibody test is typically a few hours, the time required by the testing paradigm was typically multiple days to two or more weeks. Such long delays and the accompanying anxiety clearly contributed to the nearly 30% of patients who failed to return to State counseling centers for their results.

Rapid HIV diagnosis began to assume particular importance as effective, combination antiretroviral therapy became available. Combination therapy is more effective when given immediately following exposure to HIV and it clearly reduces the risk of vertical and occupational HIV transmission while improving the quality of life and the longevity of people infected with HIV disease.

Significant reduction in the lag time between risk exposure and the availability of testing results required the evolution of a new approach to HIV testing – the rapid HIV test. These tests are widely available internationally, including six that have been approved by the United States Food and Drug Administration (FDA). The recent introduction of Clinical Laboratory Improvement Act (CLIA) waived HIV rapid test kits has allowed widespread availability of point-of-care (POCT) HIV testing with turn-around-times of 20 to 40 minutes.

Integration of rapid HIV testing into daily practice at the point-of-care allows prompt diagnosis of patients with HIV disease. These patients can then be referred to a provider with experience and expertise treating HIV patients. In addition, these patients can be referred for prevention and social services. More detailed information on the clinical aspects of rapid HIV testing is included

in the first part of this article, "Rapid Diagnostic HIV Testing: Clinical Implications."

### **RAPID DIAGNOSTIC HIV TESTS**

Rapid HIV tests to detect HIV antibody are designed to allow health care providers to supply definitive negative and preliminary positive results in a few minutes at the time of an initial patient visit. In comparison, traditional enzyme immunoassays (EIAs) operate with a paradigm that requires specimen transmittal to a laboratory, the creation of batches of specimens for efficient, cost-effective processing, the use of expensive, semi-automated or automated equipment, and the presence of significant operator expertise to perform properly and reliably. These requirements often delay results from reaching the patient for as much as 1-2 weeks.<sup>22</sup> Rapid HIV tests are comparable in sensitivity and specificity to traditional EIAs, but can be performed by testing personnel with limited technical expertise in as little as 10 minutes.

A number of HIV tests are being used worldwide. In the United States, six rapid HIV tests have received FDA approval:

- The Single Use Diagnostic System for HIV-1 (SUDS, Abbott Laboratories, Abbott Park, IL – no longer marketed),
- OraQuick® HIV-1 (OraSure Technologies, Bethlehem, PA),
- OraQuick® Advance HIV-1/HIV-2 (OraSure Technologies, Bethlehem, PA),
- Reveal™ (MedMira Laboratories, Halifax, Nova Scotia),
- Uni-Gold™ Recombigen® HIV (Trinity Biotech plc, Wicklow, Ireland), and
- Multispot HIV-1/HIV-2 (Bio-Rad Laboratories, Hercules, CA),

Additional rapid HIV tests are under FDA consideration. Many of the candidate rapid HIV tests are designed for use with a variety of specimen samples, including: serum, whole blood, plasma and/or oral mucosal transudate (OMT). Using whole blood, the five currently available FDA-approved rapid HIV tests have sensitivities ranging from 95.3% to 100% and specificities ranging from 96.7% to 100%. Performance results of six commercially available rapid HIV tests, using plasma as the test specimen, demonstrate sensitivities ranging from 96.7% to 100% and specificities ranging from 98.5% to 100%.<sup>9</sup>

The sensitivity and specificity of most rapid assays are comparable to those of non-rapid EIAs. In low prevalence settings, the predictive value of a single rapid HIV negative test result is very high. Hence, a negative rapid HIV test does not require further testing, and negative results with result-specific counseling can be provided to most people at the time of their initial visit. However,

because the positive predictive value varies with prevalence of HIV infection in the population tested, the positive predictive value will be low in populations with low prevalence.<sup>23</sup> This phenomenon has led to a testing strategy that requires a reactive EIA or rapid HIV test to be confirmed by a second, independent supplemental test.<sup>24</sup> In studies conducted outside the United States, specific combinations of two or more different rapid HIV assays have provided results as reliable as those from the EIA/western blot combination that is currently in widespread use.<sup>25</sup> In the United States, current recommendations require confirmatory testing to be conducted utilizing a Western blot or an immunofluorescence assay.<sup>26</sup>

The “window” of HIV diagnosis is dependent upon the diagnostic approach utilized to detect its presence. Following exposure, entry of the HIV virus into the bloodstream typically occurs within 3 to 7 days, while detectable HIV-1 RNA can be demonstrated 7 to 14 days later. A detectable p24 antigen may be present between 12 to 19 days, but antibody seroconversion and detection occurs between 30 to 60 days post-exposure. The onset of symptoms typically occurs 3 to 4 weeks post-exposure and most patients are symptomatic with a flu-like illness at the time of antibody seroconversion.

The ease of performing some rapid HIV tests led their manufacturers to seek and be granted waived test status under the federal Clinical Laboratory Improvement Amendments (CLIA). However, in order to ensure a high-quality testing environment, the FDA has limited the test to registered laboratories, and requires that the facility institute a quality assurance program. Guidelines from the Centers for Disease Control and Prevention (CDC) recommend participation in a proficiency testing program.<sup>22</sup>

Preliminary positive rapid tests need to be confirmed with a Western blot or immunofluorescent antibody (IFA) test. For cases such as women in labor, occupational, and non-occupational exposures prophylaxis with antiretroviral agents should be started while the confirmatory test results are pending.<sup>17,19,21</sup>

### **RAPID HIV TESTING LABORATORY LICENSURE REQUIREMENTS**

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

#### **Federal Regulations:**

The Centers for Medicare and Medicaid Services (CMS) regulates 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 1967. 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.”

In 1992, CLIA implemented regulations based upon the complexity of the lab methodology dividing laboratory testing into groups that are 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.

#### **State Regulations:**

With the exception of small group practices, numbering less than 4 physicians, clinical group practices and other organizations performing clinical laboratory testing are required to have a State of New Jersey Clinical Laboratory License. New Jersey regulations recognize only the original CLIA list of waived tests, not the complete list currently waived under federal regulations.

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 furthermore require laboratories to participate in appropriate proficiency testing.

### **INTERPRETATION OF RAPID HIV TEST RESULTS**

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 may have 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 or an immunofluorescence assay (IFA). 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.<sup>12</sup>

### **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 clients because sufficient time needs to elapse in order for development of the antibodies that are detected by the test.<sup>13,14</sup>



## 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.<sup>14</sup>

## CONCLUSION

Rapid diagnostic HIV testing will improve the proportion of patients who receive their test results, help with clinical decision making regarding the use of short course antiretroviral therapy to reduce the risk of vertical HIV transmission for women who present in labor with unknown HIV status, and to help determine the need for post-exposure prophylaxis for potential occupational and nonoccupational exposures to HIV.<sup>16,17,21</sup> As HIV counseling, testing, and referral advance, it is imperative that adjustments be made in recommendations and practices.

Rapid diagnostic HIV testing can be performed at the point of patient care. It offers clinicians an option to do on-site rapid HIV testing and provide patients with results in 20 to 40 minutes. Persons found to be infected with HIV should be referred for medical care by a provider with experience and expertise treating HIV disease, be referred for prevention services, and be referred for social services. HIV/AIDS reporting requirements should be followed.

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## CME QUIZ

### RAPID HIV TESTING: A NEW DIAGNOSTIC TOOL FOR HIV DETECTION AND ITS CLINICAL IMPLICATIONS:

To receive CME credit: fill in the form on the next page, circling correct answers, and mail or fax to us.

- Which of the following is an advantage of rapid HIV testing?
  - Increases the likelihood that a patient will seek HIV counseling and testing
  - Increases the number of patients who receive their HIV results
  - Increases the proportion of HIV-infected patients who enter treatment
  - Increases adherence to antiretroviral therapy in HIV-infected patients
- Which of the following patients should be offered antiretroviral agents to reduce the risk of transmission based on a preliminary positive rapid HIV test?
  - A man who presents with a sexually transmitted disease
  - A patient with a history of injection drug use
  - A ward clerk on a unit that has an HIV infected patient
  - A woman in active labor
- Which of the following patients should be offered HIV counseling and testing?
  - Pregnant women
  - Persons with a possible acute occupational exposure
  - Patients with a known sexual or needle-sharing exposure to the virus
  - All of the above
- The Centers for Disease Control and Prevention currently recommends that all providers integrate HIV counseling and testing into routine practice.
  - True
  - False
- Which of the following describes the NJDHSS recommendations in its standard of care for women who present in labor with unknown HIV Status?
  - Mandatory HIV counseling and mandatory HIV rapid testing of the woman
  - Mandatory HIV counseling and voluntary HIV rapid testing of the woman
  - Mandatory HIV counseling and mandatory HIV rapid testing of the newborn
  - No HIV testing of the mother or the newborn
- Which test can be used to confirm a preliminary positive rapid HIV diagnostic test?
  - A Western Blot
  - Another enzyme immunoassay (EIA)
  - Repeat testing with the same brand of rapid test
  - Viral load polymerase chain reaction test
- 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?
  - Hospitals
  - Federally Qualified Health Care Centers
  - Physician practices with less than 4 physicians
  - New Jersey Department of Health and Senior Services funded counseling and testing site
- To conduct rapid HIV testing a laboratory must be CLIA certified.
  - True
  - False
- Which of the following should be included in the posttest counseling session of a patient with a preliminary positive HIV rapid test?
  - Explain that this is a preliminary test results 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.
  - All of the above
- Which of the following is the percentage of adults in the United States who obtain an HIV test each year?
  - 7-9%
  - 10 – 12%
  - 13-15%
  - 16-18%

### RESOURCES: RAPID HIV TESTING

- Schedule a free 1-hour HIV medical education program at your health care site on **Rapid HIV Testing!** Contact Debra Bottinick at (609) 921-6622 or [DBOTTINICK@ACADEMYCME.ORG](mailto:DBOTTINICK@ACADEMYCME.ORG)
- Visit the new NJDHSS-DHAS website to find 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](http://www.state.nj.us/health/aids/rapidtesting/index.shtml)
- Visit the CDC Rapid HIV Testing website to find 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/](http://www.cdc.gov/hiv/rapid_testing/)

University of Medicine and Dentistry of New Jersey  
Center for Continuing and Outreach Education

**RAPID DIAGNOSTIC TESTING FOR HIV: CLINICAL IMPLICATIONS OF A NEW DIAGNOSTIC TOOL**

Registration Form

In order to obtain AMA PRA category 1 credit, participants are required to:

- (1) Read the learning objectives, and review the activity, and complete the self-assessment.
- (2) Complete this registration form and the activity evaluation form on the reverse side, 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 a passing score of 70% or more is achieved, a CME credit letter awarding AMA/PRA category 1 credit 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.

This activity will be posted online at <http://ccoe.umdj.edu/aids>

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

SELF-ASSESSMENT TEST

Circle the best answer for each question on page 10.

- |            |            |             |
|------------|------------|-------------|
| 1. A B C D | 4. A B     | 7. A B C D  |
| 2. A B C D | 5. A B C D | 8. A B      |
| 3. A B C D | 6. A B C D | 9. A B C D  |
|            |            | 10. A B C D |

**REGISTRATION**

First Name \_\_\_\_\_ M.I. \_\_\_\_\_ Last Name \_\_\_\_\_ Degree \_\_\_\_\_

Social Security # \_\_\_\_\_ (for credit recording purposes only)

Daytime Phone # \_\_\_\_\_ Evening Phone # \_\_\_\_\_

Fax # \_\_\_\_\_ E-mail \_\_\_\_\_

Preferred Mailing Address: Home Business

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ Zip Code \_\_\_\_\_

Affiliation, Specialty \_\_\_\_\_

I attest that I have completed the activity as designed and I am claiming [up to 1 credit] \_\_\_\_\_ AMA/PRA category 1 credit

Signature \_\_\_\_\_ Date \_\_\_\_\_

**Credit for this activity is available until February 15, 2006**  
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**Phone: 973-972-4267 or 1-800-227-4852**



**University of Medicine and Dentistry of New Jersey  
Center for Continuing and Outreach Education**

**RAPID DIAGNOSTIC TESTING FOR HIV: CLINICAL IMPLICATIONS OF A NEW DIAGNOSTIC TOOL**

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

CME

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:	Strongly Agree		Strongly Disagree		
Objective 1: Recognize the clinical diagnostic role of rapid HIV testing.	5	4	3	2	1
Objective 2: Understand the role of rapid HIV testing to reduce the risk of vertical transmission when women present in labor with unknown HIV status.	5	4	3	2	1
Objective 3: Assess if rapid HIV testing can be integrated into their practice setting.	5	4	3	2	1
Objective 4: Define when preliminary positive rapid test results can be used to start antiretroviral therapy.	5	4	3	2	1
Objective 5: Discuss confirmatory HIV testing for preliminary positive rapid test results.	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.

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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:

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CE Activity Code: o6HCo2

## IMPACT OF THE NEW GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN HIV-1-INFECTED ADULTS AND ADOLESCENTS

### TARGET AUDIENCE:

This activity is designed for physicians and nurses.

### STATEMENT OF NEED

Antiretroviral therapy (ART) for treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection has improved steadily since the advent of combination therapy in 1996. New drugs have been approved, offering added dosing convenience and improved safety profiles, while increasing drawbacks are reported with earlier drugs. Resistance testing is used more commonly in clinical practice and interactions among antiretroviral agents and with other drugs have become more complex.

The Panel on Clinical Practices for Treatment of HIV (the Panel), convened by the Department of Health and Human Services (DHHS), develops and updates guidelines which outline current understanding of how clinicians should use antiretroviral drugs to treat adults and adolescents with HIV infection. The current guidelines include revised recommendations for the initiation of antiretroviral medication, and summarize preferred regimens vs. combinations that should be avoided. Clinicians who treat patients with HIV infection and AIDS need continuous updates on HIV/AIDS treatment strategies to meet the standards of care set by these guidelines.

### LEARNING OBJECTIVES:

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

- Identify changes in the guideline for the use of antiretroviral agents in HIV-1-infected adults and adolescents.
- Discuss implications for clinical practice stemming from the changes in the guidelines.
- Discuss the potential impact on patients new to and currently receiving ART.

### 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 consisting of a series of multiple-choice and True/False questions.

The activity is complemented with references that contain the rationale for the correct answer to each question as well as/a description identifying the section of the activity that contains the correct answer, allowing participants to review the material as needed, thus finalizing their educational participation.

Upon completing this activity as designed and achieving a passing score 70% or more on the self-assessment test, participants will receive a CME credit letter awarding AMA/PRA category 1 credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials.

Estimated time to complete this activity as designed is 1 hour.

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 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

The activity was prepared in accordance with the ACCME Essentials.

This activity was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Dion Richetti, DC, Patricia Kloser, MD, MPH and Bonnie Abedini, BSN

### FACULTY:

Stephen Smith, MD

Dr. Stephen Smith is the Chief of Infectious Diseases at Saint Michael's Medical Center, where he is also the Medical Director of the Peter Ho Memorial Clinic.

Ivan Soosaipillai, MD

Dr. Ivan Soosaipillai is a first-year infectious diseases fellow at St. Michael's Medical Center via the Seton Hall University School of Graduate Medical Education, where he completed his internal medicine residency.

### DISCLOSURE:

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, all program faculty are required to disclose to the activity participants: 1) the existence of any financial interest or other relationships with the manufacturers of any commercial products/devices, or providers of commercial services, that relate to the content of their presentation/material, or the commercial contributors of this activity, that could be perceived as a real or apparent conflict of interest; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/device not yet approved.

### FACULTY DISCLOSURE DECLARATIONS:

Stephen Smith, MD, has the following financial relationships to disclose: Speaker's Bureau: GlaxoSmithKline, Merck

Ivan Soosaipillai, MD, has no financial relationships to disclose.

Field Testers

Bonnie Abedini, BSN, RN has no financial relationships to disclose.

Patricia Kloser, MD, MPH has the following financial relationships to disclose: Speaker's Bureau: GlaxoSmithKline, Roche, Glaxo; Consultant: Gilead, Boeinger Ingleheim

### 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.

### DISCLAIMER:

The views expressed in this activity are those of the faculty. It should not be inferred or assumed that they are expressing the views of NJDHSS-Division of HIV/AIDS Services, UMDNJ, or any manufacturer of pharmaceuticals.

The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult the full prescribing information on any agent(s) presented in this activity for recommended dosage, indications, contraindications, warnings, precautions, and adverse effects before prescribing any medication. This is particularly important when a drug is new or infrequently prescribed.

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### GRANTOR ACKNOWLEDGEMENT:

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."



Stephen M. Smith, MD

## IMPACT OF THE NEW GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN HIV-1-INFECTED ADULTS AND ADOLESCENTS

Ivan Soosaipillai, MD and Stephen M. Smith, MD  
Saint Michael's Medical Center  
Newark, New Jersey

### Learning objectives:

1. Identify changes in the Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents.
2. Discuss implications for clinical practice stemming from the changes in the guidelines.
2. Discuss the potential impact on patients new to and currently receiving ART.

The Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents are developed by the Panel on Clinical Practices for Treatment of HIV (Panel) and compiled by the Department of Health and Human Services (DHHS). The Guidelines outline the current understanding of how clinicians should use antiretroviral drugs and laboratory testing to treat and manage Human Immunodeficiency Virus type 1 (HIV-1) infection. The Panel, currently led by Drs. John G. Bartlett and H. Clifford Lane, meets monthly via teleconference to review new data and, when deemed needed, produces revisions or updates. Since the first publication in 1998, 12 versions of the Guidelines have been released; the latest was published on-line at <http://aidsinfo.nih.gov> on October 29, 2004. Recommendations are based upon analysis of multiple trials and expert opinions. The Panel assigns each recommendation a letter and a Roman numeral. The letter indicates the strength of the recommendation based on the expert opinion of the Panel and the Roman numeral indicates the quality of the available evidence, AI being the highest rating and DIII or E the lowest. When significant data is not available, or inconclusive, then the recommendations are based on expert opinion.

Upon entering a clinic or private practice, each HIV<sup>+</sup> patient undergoes an initial evaluation. The Panel recommends the following baseline laboratory studies:

- HIV antibody testing (if laboratory confirmation not available);
- CD4<sup>+</sup> T-cell count;
- Plasma HIV RNA;
- Complete blood count, chemistry profile, transaminase levels, BUN and creatinine, urinalysis, RPR or VDRL, tuberculin skin test (unless a history of prior tuberculosis or positive skin test), *Toxoplasma gondii* IgG, Hepatitis A, B, and C serologies, and PAP smear in women.

In addition, patients, who are have risk factors for diabetes and/or cardiovascular disease, should have a fasting blood glucose and serum lipids measured. An area of controversy is baseline testing for viral drug resistance (see below). In drug naïve patients, it is unclear whether genotyping or phenotyping, performed prior to the initiation of therapy, would affect outcome.

Once the baseline CD4 cell count and plasma HIV RNA (often referred to as the viral load) are known, the physician and patient should consider treatment based on the following recommendations:

- Antiretroviral therapy is recommended for all patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4<sup>+</sup> T cell count.
- Antiretroviral therapy is also recommended for asymptomatic patients with <200 CD4<sup>+</sup> T cells/mm<sup>3</sup>.
- Asymptomatic patients with CD4<sup>+</sup> T cell counts of 201-350 cells/mm<sup>3</sup> should be offered treatment.

- For asymptomatic patients with CD4<sup>+</sup> T cell of >350 cells/mm<sup>3</sup> and plasma HIV RNA >100,000 copies/ml most experienced clinicians defer therapy but some clinicians may consider initiating treatment.
- Therapy should be deferred for patients with CD4<sup>+</sup> T cell counts of >350 cells /mm<sup>3</sup> and plasma HIV RNA <100,000 copies/mL.

These recommendations for the initiation of therapy have changed slightly since the previous version of the Guidelines. The plasma HIV RNA level cut-off for asymptomatic patients with a CD4 cell count above 350 cells/mm<sup>3</sup> has been raised from 55,000 to >100,000 copies/ml. The ART Cohort Collaboration study that included 13 studies from Europe and North America, showed that viral load at commencement of therapy was associated with subsequent clinical progression only if it is greater than or equal to 100,000 copies/ml. Additionally, a recent collaborative analysis of three cohort studies showed that patients with baseline viral loads of greater than 100,000 copies/ml had a lower rate of achieving viral suppression than those with less than this number. Many providers have already adopted this “wait and watch” approach with patients, who have good CD4<sup>+</sup> T-cell counts. We now know that delaying therapy in most of these patients until their CD4<sup>+</sup> counts fall causes no harm. Additionally, when a patient delays therapy, the long-term toxicities associated with HIV therapy may be reduced and his/her quality of life improved.

The Panel also makes recommendations on the different, available therapeutic regimens for treatment of naïve or experienced patients. The Panel classifies regimens as Preferred or Alternative and also recommends against the use of some medications. For patients naïve to HIV therapy, the Panel recommends either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI) based regimens with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs).

As the preferred NNRTI based regimens, the Panel recommends efavirenz + (zidovudine or tenofovir) + (lamivudine or emtricitabine). An alternative NNRTI-based regimen is efavirenz + (didanosine or abacavir or stavudine) + (lamivudine or emtricitabine). Efavirenz is a proven teratogen in macaques, should not be used in pregnant women, and should be used with caution in women of childbearing age. Nevirapine<sup>®</sup>, another NNRTI, may also be used. However, recent data show that Nevirapine<sup>®</sup> causes substantial liver toxicity in patients with good CD4<sup>+</sup> T-cell counts, particularly in women, whose CD4<sup>+</sup> T-cell count is > 250 cells/mm<sup>3</sup>. For men, increased nevirapine liver toxicity is seen, when their CD4<sup>+</sup> T-cell counts are > 400 cells/mm<sup>3</sup>. The Panel recommends against the use of delavirdine, the third FDA approved NNRTI.

For PI-based regimens, the preferred initial combination is lopinavir/ritonavir (co-formulated as Kaletra<sup>®</sup>) + zidovudine + (lamivudine or emtricitabine). Alternative regimens are many and include:

- Atazanavir, fosamprenavir, ritonavir-boosted fosamprenavir, ritonavir-boosted indinavir, nelfinavir, or ritonavir-boosted saquinavir - all used in combination with (zidovudine or stavudine or tenofovir or abacavir or didanosine) + (lamivudine or emtricitabine)
- Lopinavir<sup>®</sup>/ritonavir + (abacavir or stavudine or tenofovir or didanosine) + (lamivudine or emtricitabine)

Ritonavir is used in each of these regimens to increase or “boost” the level of the active PI. Atazanavir, an azapeptide, has fewer effects on lipids than other PIs and is given once daily with or without ritonavir-boosting. However, since boosted atazanavir has, to date, only been studied in drug-experienced patients, the Panel does not recommend the use of ritonavir-boosted atazanavir in treatment-naïve patients, unless combined with tenofovir, which lowers atazanavir levels. The Panel does not comment on the use of regimens containing two active protease inhibitors.

The major changes in these recommendations affect the selection of the dual nucleoside backbone. It is noted that certain drugs are very similar, for example lamivudine and emtricitabine, and that they should not be combined together. Tenofovir plus lamivudine or emtricitabine is now recommended as a 2-NRTI backbone for both NNRTI and PI-based regimens. Previously, this recommendation was limited to NNRTI-based regimens only. The other change in recommendation was the removal of stavudine from “preferred” to “alternative”, due to increasing reports of stavudine associated toxicities, including peripheral neuropathy, lipoatrophy, and hyperlipidemia. Stavudine with didanosine should not be used together, due to additive toxicity and zidovudine with stavudine should also be avoided due to intracellular interactions that decrease their antiviral activities. The Panel does not make a recommendation regarding the continued use of stavudine in patients who are virologically suppressed and not also on didanosine. Of note, hydroxyurea, which is not FDA approved for the treatment of HIV, will no longer be listed as a potential therapeutic in the Guidelines.

As before, triple NRTI regimens should only be used if the patient cannot tolerate a NNRTI- or PI-based regimen. Further, the sole triple NRTI regimen that the Panel recommends using is zidovudine + abacavir + lamivudine. The Panel recommends against the use of other triple NRTI regimens, such as abacavir + tenofovir + lamivudine or didanosine + tenofovir + lamivudine, as recent studies have shown unacceptably high failure rates with these regimens.

Testing for HIV resistance to antiretroviral drugs is a useful tool for guiding antiretroviral therapy. There are two types of drug resistance testing, genotyping and phenotyping. The Panel does not prefer one form of testing, but recommends resistance testing be performed before changing therapy in a patient, who was virologically suppressed and now is not. The clinical data are most strong in this scenario of virologic failure. In patients naïve to drug therapy, it is unclear if resistance testing helps. Despite the increased use of antiretroviral therapy in the community, the frequency of drug resistance mutations in patients, naïve to therapy, is still quite low. Acutely infected patients may benefit from resistance testing, since the virus has had little time to revert towards wild type. Additionally, since certain mutations, such as key NNRTI resistance mutations, may persist for long periods in the absence of drug pressure, patients, who have been infected for 1-3 years, may also benefit. Finally, if it is probable that the patient was infected through contact with a person known to take antiretroviral drugs, one may consider resistance testing. For example, at the Peter Ho Memorial Clinic at Saint Michael's Medical Center in Newark, we performed resistance testing on a treatment-naïve patient. We knew the probable source had been exposed to antiretrovirals. Both genotyping and phenotyping confirmed that this treatment-naïve patient's virus was resistant to all protease inhibitors.

Virologic failure occurs often and for a number of reasons, including incomplete drug adherence, sub-optimal pharmacokinetics (i.e. unsuspected drug-drug interactions), high baseline viral load, active substance abuse, and unknown reasons. Virologic failure is defined by the Panel as "*HIV RNA level >400 copies/mL after 24 weeks, >50 copies/mL after 48 weeks, or a repeated HIV RNA level >400 copies/mL after prior suppression of viremia to <400 copies/mL.*" In treating patients with virologic failure, the clinician should review the adherence issues, side effects, potential pharmacokinetic problems, and suspected drug resistance. When changing the drug regimen for treatment failure the Panel recommends:

- For the patient with virologic failure, perform resistance testing while the patient still is taking the drug regimen or within 4 weeks after regimen discontinuation.
- Use the treatment history and past and current resistance test results to identify active agents (preferably 3 or more) to design a new regime).
- If three active agents cannot be identified, consider pharmacokinetic enhancement of protease inhibitors (with the exception of nelfinavir) with ritonavir and/or re-using other prior antiretroviral agent).

- Adding a drug with a new mechanism of action (e.g. HIV entry inhibitor) to an optimized background antiretroviral regimen can add significant antiretroviral activity.
- In general, one active drug should not be added to a failing regimen because drug resistance is likely to develop quickly. However, in patients with advanced HIV disease (e.g. CD4 <100) and higher risk of clinical progression, adding one active agent (with an optimized background regimen) may provide clinical benefits and should be considered.

Drug resistance mutations may not be detectable in the absence of continued drug pressure. For example, the M184V mutation, which confers high-level resistance to lamivudine and emtricitabine, may fall below the level of detection in a matter of weeks, once lamivudine or emtricitabine is discontinued. However, this resistant virus persists as a minority viral species and quickly will re-appear if the drug is restarted. For this reason, the provider must perform drug testing, while the patient is still on his/her most recent regimen and must consider which drugs the patient had been taking in the past and may have failed. Together, resistance testing and historical information can then be used to choose the drugs most likely to be effective.

The Guidelines also have sections on three areas of interest: therapeutic drug monitoring (TDM), discontinuation of antiretroviral therapy, and management of acute HIV infection. Each of these areas lacks sufficient data for the Panel to give strong recommendations. However, these sections provide the reader with analyses of the available information and expert opinions.

- TDM of PIs and NNRTIs may be warranted in certain situations, since plasma concentrations are commercially available, correlate with response to therapy, and can vary significantly for a variety of reasons. TDM of NRTIs is still considered a research tool only.
- Clinicians discontinue therapy frequently, even in patients who are virologically suppressed. The Guidelines advise caution in discontinuing efavirenz and nevirapine, which each has a long half-life. Some recommend stopping the NNRTI first and continuing the 2-NRTIs for a period of time to minimize the chance of drug resistance developing. The Panel also cautions providers against stopping lamivudine, emtricitabine, or tenofovir in patients who are chronically infected with hepatitis B virus. Each of these three potentially inhibits hepatitis B virus and sudden discontinuation of hepatitis B virus therapy can result in an acute exacerbation or hepatic flare. Patients in this category should be monitored closely. Some experts recommend the addition of adefovir to treat the hepatitis B virus infection.



- Therapy of acute HIV infection may theoretically improve the long-term outcome. However, data are again lacking. Potential benefits include lower viral load set point and slower loss of CD<sub>4</sub><sup>+</sup> T-cells. Potential drawbacks include the adverse reactions to the drug regimen and induction of drug resistant virus. Further, the optimal duration of treatment is not known. Therefore, treatment of acute HIV infection is considered optional.

The Guidelines provide invaluable information and recommendations to clinicians who care for HIV<sup>+</sup> patients. The recommendations are carefully made and the relevant references are listed. The recent changes in the Guidelines should not significantly affect how an experienced practitioner cares for his/her patients, because many of us have already adopted the changes. The breadth and length (115 pages) of the Guidelines re-enforce to the reader that the treatment and management of HIV is the most complicated medical treatment, bar none. As the literature supports and recent societies recommend, HIV<sup>+</sup> patients should be treated by experienced clinicians, who have access to expert consultants and stay current on the latest advances in the field.

### CASE SCENARIO #1:

After being recently diagnosed as HIV<sup>+</sup>, a 45 year-old man presents to your practice for treatment. The patient has no other medical problems. He has no family history of diabetes or significant cardiovascular disease. The patient denies smoking. He is slightly overweight. His baseline CD<sub>4</sub><sup>+</sup> T-cell count and viral load are 482 cells/mm<sup>3</sup> and 88,632 copies/ml respectively.



- Q. Does this patient require anti-retroviral therapy?
- A. No. His CD<sub>4</sub><sup>+</sup> T-cell count is > 350 cells/mm<sup>3</sup> and his viral load is <100,000 copies/ml. Therefore, according to the current Guidelines, he should have his CD<sub>4</sub><sup>+</sup> T-cell count and viral load measured every 3-4 months. If his viral load increases to > 100,000 copies/ml or when his CD<sub>4</sub><sup>+</sup> T-cell count falls to < 350 cells/mm<sup>3</sup>, then he should be offered therapy. This patient's CD<sub>4</sub><sup>+</sup> T-cell count will decrease by an estimated 60-80 cells/mm<sup>3</sup> per year. However, therapy will be just as effective if it is delayed until then.

### CASE SCENARIO #2:

A 58 year-old woman is referred to you by her primary care physician, after she tested positive for HIV. The patient is obese and is on therapy for primary hypertension. Her family history is significant for diabetes and for early cardiovascular disease. She reports a long history of smoking tobacco. She denies recreation drug use. Baseline labs show that her viral load is 354,000 copies/ml and her CD<sub>4</sub><sup>+</sup> T-cell count is 389 cells/mm<sup>3</sup>.

- Q. Should this patient be offered therapy?
- A. Yes. Since her viral load is > 100,000 copies, antiretroviral therapy is indicated.
- Q. Which regimen should she be offered?
- A. The patient is obese and has a family history for diabetes and cardiovascular disease. Therefore, a PI-based regimen may not be best suited for her. The preferred NNRTI regimens are efavirenz + (lamivudine or emtricitabine) + (zidovudine or tenofovir). The patient, if she wishes to go on therapy, should undergo extensive pre-treatment counseling, which should include warnings about potential adverse drug reactions. Efavirenz can cause significant CNS events, such as dizziness, somnolence, insomnia, abnormal dreams, confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. These adverse symptoms usually subside spontaneously after 2-4 weeks.
- A. Alternatively, a ritonavir boosted-PI based regimen may be used. Pre-treatment serum lipids and a fasting blood glucose should be measured. The patient should be educated about the potential development of diabetes mellitus and its symptoms.

### CASE SCENARIO #3:

A 28 year-old woman comes to your clinic. Her boyfriend has AIDS and she recently tested positive for HIV. She has a viral load of 14,354 copies/ml and her CD<sub>4</sub><sup>+</sup> T-cell count is 289 cells/mm<sup>3</sup>. She has no other medical problems. Her family history is not significant. She denies current pregnancy.

- Q. Should she be treated?
- A. Yes. Her CD<sub>4</sub><sup>+</sup> T-cell count is < 350 cells/mm<sup>3</sup>.
- Q. What should she be treated with?
- A. This patient is of childbearing age. Efavirenz should be used with caution in this population. A PI-based regimen is a safer choice, if the patient may become pregnant. Nevirapine is associated with increased liver toxicity in women with CD<sub>4</sub><sup>+</sup> T-cell count > 250 cells/mm<sup>3</sup>, so it should be avoided.

## CME QUIZ

### IMPACT OF THE NEW GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN HIV-1-INFECTED ADULTS AND ADOLESCENTS

To receive CME credit: fill in the form on the next page, circling the correct answers, and mail or fax to us.

1. Antiretroviral therapy is recommended for all HIV-positive patients with a history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4<sup>+</sup> T cell count.
  - a. True
  - b. False
2. Antiretroviral therapy is recommended for all asymptomatic HIV-positive patients with <200 CD4<sup>+</sup> T cells/mm<sup>3</sup>
  - a. True
  - b. False
3. Antiretroviral therapy is recommended for all asymptomatic HIV-positive patients with CD4<sup>+</sup> T cell counts of 201-350 cells/mm<sup>3</sup>
  - a. True
  - b. False
4. Therapy should not be deferred for patients with CD4<sup>+</sup> T cell counts of >350 cells/mm<sup>3</sup> and plasma HIV RNA <100,000 copies/mL.
  - a. True
  - b. False
5. The Preferred Regimen recommended by the Panel on Clinical Practices for Treatment of HIV is either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI) based regimens with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs).
  - a. True
  - b. False
6. The ART Cohort Collaboration study showed that clinical progression was associated with viral load of:
  - a.  $\geq 55,000$  copies/ml
  - b.  $\geq 75,000$  copies/ml
  - c.  $\geq 100,000$  copies/ml
  - d. no level has been established
7. The preferred NNRTI-based regimens containing efavirenz should be used with caution for women who are pregnant or of childbearing age
  - a. True
  - b. False
8. Reasons for virologic failure include:
  - a. Drug-drug interactions
  - b. Incomplete drug adherence
  - c. a and b
  - d. None of the above

9. The most effective time to use genotyping or phenotyping resistance testing is:
  - a. In drug naïve patients, prior to the initiation of therapy
  - b. For a patient with virologic failure, before changing therapy
  - c. Both
  - d. None of the above
10. The Panel advises caution to clinicians who are discontinuing lamivudine, emtricitabine, or tenofovir, to minimize the risks of:
  - a. Drug resistance
  - b. Flare-up of hepatitis B
  - c. Both
  - d. None of the above

### REFERENCES AND RESOURCES: ANTIRETROVIRAL TREATMENT

- DHHS. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents: Department of Health and Human Services; October 29, 2004. Available at <http://aidsinfo.nih.gov>
- Supplement to the DHHS Guidelines, October 29, 2004. Adherence to Potent Antiretroviral Therapy: [http://aidsinfo.nih.gov/guidelines/adult%5CAH\\_102904.pdf](http://aidsinfo.nih.gov/guidelines/adult%5CAH_102904.pdf)
- Visit the AETC National Resource Center for HIV treatment guidelines and PowerPoint slidesets with speaker notes: [www.aidsetc.org/aidsetc?page=et-30-03&catid=arvt&pid=1](http://www.aidsetc.org/aidsetc?page=et-30-03&catid=arvt&pid=1)

### MORE INFORMATION

To schedule a free 1-hour HIV medical education program at your health care site on *Diagnosis and Initial Management of HIV/AIDS: What the Primary Care Physician Should Know*, contact Debra Bottinick at (609) 921-6622 or [DBOTTINICK@ACADEMYCME.ORG](mailto:DBOTTINICK@ACADEMYCME.ORG)

University of Medicine and Dentistry of New Jersey  
Center for Continuing and Outreach Education

**IMPACT OF THE NEW GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN HIV-1-INFECTED ADULTS AND ADOLESCENTS**

Registration Form

In order to obtain AMA PRA category 1 credit, participants are required to:

- (1) Read the learning objectives, and review the activity, and complete the self-assessment.
- (2) Complete this registration form and the activity evaluation form on the reverse side, 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 a passing score of 70% or more is achieved, a CME credit letter awarding AMA/PRA category 1 credit 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.

This activity will be posted online at <http://ccoe.umdj.edu/aids>

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

SELF-ASSESSMENT TEST

Circle the best answer for each question on page 18.

- |        |            |             |
|--------|------------|-------------|
| 1. A B | 4. A B     | 7. A B      |
| 2. A B | 5. A B     | 8. A B C D  |
| 3. A B | 6. A B C D | 9. A B C D  |
|        |            | 10. A B C D |

REGISTRATION

First Name \_\_\_\_\_ M.I. \_\_\_\_\_ Last Name \_\_\_\_\_ Degree \_\_\_\_\_

Social Security # \_\_\_\_\_ (for credit recording purposes only)

Daytime Phone # \_\_\_\_\_ Evening Phone # \_\_\_\_\_

Fax # \_\_\_\_\_ E-mail \_\_\_\_\_

Preferred Mailing Address: Home Business

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ Zip Code \_\_\_\_\_

Affiliation, Specialty \_\_\_\_\_

I attest that I have completed the activity as designed and I am claiming [up to 1 credit] \_\_\_\_\_ AMA/PRA category 1 credit

Signature \_\_\_\_\_ Date \_\_\_\_\_

**Credit for this activity is available until February 15, 2006**

**UMDNJ-Center for Continuing and Outreach Education**

**PO Box 1709, Newark, NJ 07101-1709**

**Phone: 973-972-4267 or 1-800-227-4852**

**CE Activity Code: o6HC03**

**University of Medicine and Dentistry of New Jersey  
Center for Continuing and Outreach Education**

**IMPACT OF THE NEW GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN HIV-1-INFECTED ADULTS AND ADOLESCENTS**

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

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:	Strongly Agree		Strongly Disagree		
Objective 1: Identify changes in the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.	5	4	3	2	1
Objective 2: Discuss implications for clinical practice stemming from the changes in the guidelines.	5	4	3	2	1
Objective 3: Discuss the potential impact on patients new to and currently receiving ART.	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.

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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:

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**CE Activity Code: o6HC03**

## IN THE NEWS!

### FDA warns consumers not to use home-use diagnostic test kits that have been marketed via the Internet by Globus Media for HIV, syphilis and some drugs, as results may not be accurate.

<http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01340.html>

February 11, 2005 -The Food and Drug Administration (FDA) is warning consumers not to use unapproved home-use diagnostic test kits that have been marketed nationwide via the Internet by Globus Media, Montreal, Canada. The use of these products could result in false results (though there is no confirmed evidence of false positives) that could lead to significant adverse health consequences.

The illegal kits are labeled as:

- Rapid HIV Test Kit
- Rapid Syphilis Test Kit
- One Step Cassette Style Cocaine Test
- One Step Cassette Style Marijuana (THC) Test
- One Step Cassette Style Amphetamine Test
- Rapid Dengue Fever Test
- One Step Midstream Style HCG Urine (Home)
- Pregnancy Test

#### FDA learned of the problem from two consumer complaints.

FDA has not approved or evaluated the performance of any of Globus Media's products. As a result, consumers cannot know with any degree of certainty that test results are correct. For example, a person testing positive for HIV (human immunodeficiency virus, or the AIDS virus) using one of these tests may not

be infected with HIV, or, worse, someone infected with HIV may test negative and not seek medical treatment or spread the virus to others.

The tests were sold through web sites and distributed throughout the U.S., usually by overnight delivery services. These have been made available for sale on several web sites, including [www.htkit.com](http://www.htkit.com) and [www.hstkits.com](http://www.hstkits.com). The kits usually are contained in a paper envelope with instructions inside the packaging. The envelope, instructions and packaging may not accurately identify the manufacturer, packer or distributor. The name of the kit appears on the instructions.

Consumers who have these products should not use them. Anyone who has used one of these test kits should be retested using valid test methods. Only one HIV home collection test system is approved by FDA and legally sold in the United States. This test, sold as either "The Home Access HIV-1 Test System" or "The Home Access Express HIV-1 Test System" is manufactured by Home Access Health Corporation and allows blood samples to be taken at home which people then send to a laboratory for testing. No home-use test kits intended for diagnosing syphilis and dengue fever are approved for sale in the U.S.

The FDA has issued an import alert which alerts FDA field personnel to the possible importation of these devices, provides guidance as to their detention and refusal of admission into the U.S., and also advises U.S. Customs officials about these products.

### COST-EFFECTIVENESS OF SCREENING FOR HIV

February 10, 2005. New England Journal of Medicine (abstract summary of study by Yale, Harvard, and University of California researchers re: *Expanding HIV testing beyond identified "at-risk" populations*)

The authors estimate that routine HIV screening in health care settings with a 1 percent prevalence of HIV infection costs about \$15,000 per quality-adjusted life-year gained. The cost remains below \$50,000 when the prevalence of HIV is above 0.05 percent. When the potential benefits of reduced HIV transmission are excluded, screening populations with a 1 percent prevalence of HIV infection costs about \$42,000 per quality-adjusted life-year gained.

Routine screening for HIV is cost-effective, except in settings with an extremely low prevalence of HIV infection.

### HIV/AIDS MEDICAL UPDATE SERIES: FREE ON-SITE TRAINING

This free series has been extended. Call or e-mail to schedule a 1-hour HIV medical education program at **your health care site**, and to find out about obtaining CME/CE credit for physicians and nurses. Complete a brief request form available from Debra Bottinick at (609) 921-6622 or [DBOTTINICK@ACADEMYCME.ORG](mailto:DBOTTINICK@ACADEMYCME.ORG)

**Sponsors:** Center for Continuing and Outreach Education-Division of AIDS Education at UMDNJ (UMDNJ-CCOE-AIDS), and the American Academy of CME, Inc. (AACME), with funding from the New Jersey Department of Health & Senior Services, Division of HIV/AIDS Services.

#### Topics available:

- 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
- 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 HIV Testing

# INFLUENZA (FLU)

## INFORMATION FOR PERSONS WITH HIV/AIDS

Sindy M. Paul, M.D., M.P.H., Linda Berezny, R.N., Katherine Wytovich

### Introduction

People with HIV/AIDS are considered at increased risk from serious influenza-related complications. Studies have shown an increased risk for heart and lung-related hospitalizations in people infected with HIV during influenza season as opposed to other times of the year, and a higher risk of influenza-related death in HIV infected people. Other studies have indicated that influenza symptoms might be prolonged and the risk of influenza-related complications higher for certain HIV infected people. Vaccination with a flu shot has been shown to produce an immune response against influenza viruses in certain people infected with HIV.

Because influenza can result in serious illness, HIV infected persons are recommended for vaccination. In the setting of the current vaccine shortage, people with HIV/AIDS are among the priority groups that should get flu shots this season.

### Should people with HIV/AIDS receive the inactivated influenza vaccine?

People with chronic underlying medical conditions, including HIV/AIDS, should receive inactivated influenza vaccine (the flu shot) during the 2004-05 influenza season. People with HIV/AIDS are considered at increased risk from serious influenza-related complications and should be vaccinated. Persons with advanced HIV disease may have a poor response to immunization. Therefore, in addition to vaccination, chemoprophylaxis (use of antiviral medications for prevention) should be considered for these patients if they are likely to be exposed to people with influenza. (CDC has developed interim recommendations on the use of antiviral medications for the 2004-05 influenza season. These can be found at: <http://www.cdc.gov/flu/professionals/treatment/0405antiviralguid.htm>.)

### Are there people with HIV/AIDS who should NOT receive the inactivated influenza vaccine?

Contraindications to the use of inactivated influenza vaccine (the flu shot) in persons with HIV/AIDS are the same as those for uninfected persons including a history of severe allergy (i.e., anaphylactic allergic reaction) to hens' eggs, or a history of onset of Guillain-Barre syndrome during the 6 weeks after vaccination.

### Can people with HIV/AIDS receive the live attenuated flu vaccine (LAIV, sold commercially as FluMist)?

No. Persons with HIV/AIDS and persons with other medical conditions are not recommended to receive the live influenza vaccine. LAIV contains a weakened form of the live influenza virus. LAIV is approved for use only among healthy persons between the ages of 5 and 49 years.

### Should health-care workers who have contact with HIV/AIDS patients be vaccinated?

Influenza vaccination is recommended for health-care workers who are involved in direct care of HIV infected patients. More information about vaccination of health-care workers can be found in "Prevention and Control of Influenza Recommendations of the Advisory Committee on Immunization Practices (ACIP)" at the following website: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5306a1.htm>. Health-care workers who are healthy, less than 50 years of age, and are not pregnant may receive the nasal-spray flu vaccine (LAIV/FluMist).

**For more information, visit [www.cdc.gov/flu](http://www.cdc.gov/flu) or call CDC at (800) CDC-INFO (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY).**

### When should people with HIV/AIDS be prescribed antiviral medications for chemoprophylaxis (prevention)?

Persons at high risk of serious influenza-related complications should be given antiviral medications if they are likely to be exposed to other people with influenza. For example, when a family or household member is diagnosed with influenza, the exposed person with HIV/AIDS should be given chemoprophylaxis for 7 days. Vaccinated and unvaccinated HIV-infected persons who are residents of institutions experiencing an influenza outbreak should be given chemoprophylaxis for the duration of the outbreak or until discharge. People with advanced HIV disease who are not expected to mount an adequate antibody response to influenza vaccination should consider chemoprophylaxis with antiviral medications for the duration of influenza activity in the community, if antiviral medications are available in adequate supply locally. CDC has developed interim recommendations on the use of antiviral medications for the 2004-05 influenza season. These can be found at the following website: <http://www.cdc.gov/flu/professionals/treatment/0405antiviralguid.htm>.

There are no published data on interactions between anti-influenza agents such as amantadine and rimantadine and drugs used in the management of HIV infected persons. Patients should be observed for adverse drug reactions to anti-influenza

#### **Private Sector Sources of Influenza Antiviral Medications**

*Pharmaceutical distributors  
should be contacted  
directly for availability and  
procurement of antiviral  
medications.*

chemoprophylaxis agents, especially when neurological conditions or renal insufficiency are present.

### **2004-05 Antiviral Medications Usage Guidelines from the Centers for Disease Control and Prevention (CDC)**

CDC is issuing interim recommendations for the use of antiviral medications during the 2004-05 season. Local availability of these medications may vary from community to community, which could impact how these medications should be used.

1. CDC encourages the use of **amantadine or rimantadine for chemoprophylaxis** and **use of oseltamivir or zanamivir for treatment** as supplies allow, in part minimizing the development of resistance to the adamantane class of drugs (amantadine or rimantadine) among circulating influenza viruses.
2. **People who are at high risk of serious complications** from influenza may benefit most from antiviral medications. Therefore, in general, people who fall into these high risk groups should be given **priority for use of influenza antiviral medications:**

#### ***Treatment***

- Any person experiencing a potentially life-threatening influenza-related illness should be treated with antiviral medications.
- Any person at high risk for serious complications of influenza and who is within the first 2 days of illness onset should be treated with antiviral medications. Pregnant women should consult their primary provider regarding use of influenza antiviral medications.

**Antiviral Use in Children:** Rimantadine is approved for prophylaxis of influenza among children aged >1 year and for treatment and prophylaxis of influenza among adults. Although rimantadine is approved only for prophylaxis of influenza among children, certain specialists in the management of influenza consider it appropriate for treatment of influenza among children. Also available for treatment of children are amantadine (children aged >1 year), oseltamivir (children aged >1 year), or zanamivir (children aged >7 years).

#### ***Chemoprophylaxis***

- All persons who live or work in **institutions** caring for people at high risk of serious complications of influenza infection should be given antiviral medications in the event of an institutional outbreak. This includes nursing homes, hospitals, and other facilities caring for persons with immunosuppressive conditions, such as HIV/AIDS. When vaccine is available, vaccinated staff require chemoprophylaxis only for the 2-week period following vaccination. Vaccinated and unvaccinated residents should receive chemoprophylaxis for the duration of institutional outbreak activity. Rapid tests or other

influenza tests should be used to confirm influenza as the cause of outbreaks as soon as possible. However, treatment and chemoprophylaxis should be initiated if influenza is strongly suspected and test results are not yet available. Other outbreak control efforts such as cohorting of infected persons, and the practice of respiratory hygiene and other measures also should be implemented. For further information on detection and control of influenza outbreaks in acute care facilities, see *Detection and Control of Influenza Outbreaks in Acute Care Facilities* at [http://www.cdc.gov/ncidod/hip/infect/flu\\_acute.htm](http://www.cdc.gov/ncidod/hip/infect/flu_acute.htm).

- All persons at high risk of serious influenza complications should be given antiviral medications if they are likely to be exposed to others infected with influenza. For example, when a high-risk person is part of a family or household in which someone else has been diagnosed with influenza, the exposed high-risk person should be given chemoprophylaxis for 7 days.
3. Antiviral medications can be **considered** in other situations when the available supply of such medications is locally adequate.
    - **Chemoprophylaxis** of persons in communities where influenza viruses are circulating, which typically lasts for 6-8 weeks:
      1. Persons at high risk of serious complications who are not able to get vaccinated.
      2. Persons at high risk of serious complications who have been vaccinated but have not had time to mount an immune response to the vaccine. In adults, chemoprophylaxis should occur for a period of 2 weeks after vaccination. In children aged <9 years, chemoprophylaxis should occur for 6 weeks after the first dose, or 2 weeks after the second dose, depending on whether the child is scheduled to receive one or two doses of vaccine.
      3. Persons with immunosuppressive conditions who are not expected to mount an adequate antibody response to influenza vaccine.
      4. Health-care workers with direct patient care responsibilities that are not able to obtain vaccine.
    - **Treatment** of infected adults and children aged >1 year who do not have conditions placing them at high risk for serious complications secondary to influenza infection.
  4. Where the supplies of both influenza vaccine and influenza antiviral medications may not be sufficient to meet demand, CDC does not recommend the use of influenza antiviral medications for chemoprophylaxis of non-high risk persons in the community.

## CLINICAL TRIALS

### SMART STUDY Q&A: STRATEGIES FOR MANAGEMENT OF ANTIRETROVIRAL THERAPY

Corey Rosmarin

North Jersey Community Research Initiative (NJCRI)

Director of Clinical Research

The SMART Study is being conducted at NJCRI (North Jersey Community Research Initiative) in collaboration with the Community Programs for Clinical Research on AIDS (CPCRA). The purpose of the study is to compare two strategies of Antiretroviral Management and the long term consequences of these strategies. The **Viral Suppression Arm** is aimed at achieving virologic control immediately after randomization and through follow up. The **Drug Conservation Arm** is based on episodic use of antiretroviral treatment to maintain a CD4 cell count of greater to or equal to 250 cells/mm<sup>3</sup>.

At the moment NJCRI has enrolled 136 participants and has one of the highest adherence rates in the CPCRA. NJCRI is always asked questions about the study. Below are some of the answers to those questions.

**Q.** What have participants disclosed about their own experiences from being in the SMART study?

**A.** The participants have told us of positive experiences from being in the SMART study. The continuous contact and follow up on the clinician's part has made the participants want to be adherent to their arm, as well as feel that they are getting the attention they deserve. They have often expressed that the study has renewed their commitment to their health, which has led many participants to become advocates for the SMART Study by referring friends and loved ones to NJCRI to hear more about the study.

**Q.** Will the Viral Suppression arm or the Drug Conservation arm cause HIV resistance?

**A.** It is not yet known whether one of these groups will lead to more HIV resistance than the other. The longer a person is on antiretroviral medications, the higher chance of developing drug resistance, so there may be a lower risk of drug resistance in the Drug Conservation Arm because they will be taking medications episodically rather than continuously. But the Viral Suppression arm may have lower risk because resistance is less likely to occur when the virus is suppressed

and not able to multiply. The SMART Study will take a closer look at resistance development in both arms.

**Q.** Why should I take the antiretroviral medications if I am assigned to the Viral Suppression arm?

**A.** Keeping the viral load low and under control may prevent lasting damage to the immune system. There are many effective drug regimens and options to control the virus and prevent it from multiplying.

**Q.** Why should I stop taking my antiretroviral medications if I am assigned to the Drug Conservation arm?

**A.** Advantages to stopping medications include the possibility that there may be more treatment options later, when you may need it the most, and there will be fewer side effects because you are not on medication. If your (participant's) CD4 Count falls below 250 cells/mm<sup>3</sup>, then antiretroviral medication will be prescribed.

**Q.** What has NJCRI learned about doing the SMART study?

**A.** It is important to keep our participants informed throughout the study. We let the participants know how enrollment is going, what they can do to help enrollment and giving them updated literature on the study so they have the current and most updated materials. The participants really appreciated it because they feel they are helping their community, which makes them continue to be adherent to the study.

*\*\*If you are interested in participating in the SMART Study anywhere in NJ please contact NJCRI at 973-483-3444 and ask to speak with a Research Nurse.*

## STRATEGIES FOR MANAGEMENT OF ANTIRETROVIRAL THERAPY



# FIXED DOSE COMBINATION THERAPY:

## NEW OPTIONS FOR HIV REGIMENS

Todd P. Levin, DO

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Recently, the US Department of Health and Human Services (DHHS) once again updated the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.<sup>1</sup> As a part of these guidelines, recommendations were made regarding choice of antiretrovirals in treating patients with HIV/AIDS. This article will focus on recommendations made in the choice of the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) as the backbone of highly active antiretroviral therapy (HAART). Specifically, the article will discuss newly FDA approved fixed dose combination medications with respect to adherence, tolerability and resistance.

AIDS morbidity and mortality has dramatically decreased with the advent of HAART.<sup>2</sup> New Jersey specific data has shown improved AIDS-Free survival in the HAART era (1996-2002) versus in the pre-HAART era (1992-1995) (Figure 1).<sup>3</sup> Unfortunately, the improved morbidity has not been uniform across socio-demographic and exposure categories. AIDS-Free survival is greater in females compared to males, non-Hispanic Caucasians compared to Hispanics and non-Hispanic Blacks, patients less than 25 years old compared to older patients, and men who have sex

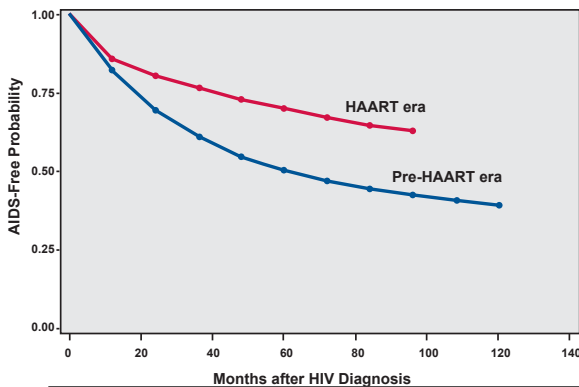


Figure 1: AIDS-Free Survival Curves: Pre-HAART (1992-1995) vs. HAART (1996-2002)

with men compared to heterosexuals and intravenous drug users.<sup>3</sup> Efforts need to be focused on patients in these specific demographic areas to improve AIDS-Free survival.

Choosing a HAART regimen that is potent, easy to tolerate, and not likely to lead to resistance is one way to improve AIDS-Free survival. Many factors need to be considered in choosing a HAART regimen, so that medication choice does not exacerbate an underlying medical condition or cause drug-drug

toxicities. These include comorbidities such as tuberculosis, liver disease, renal disease, cardiovascular disease, mental illness, and pregnancy. Dose frequency, pill burden, food and water restrictions or requirements, and side effects can all contribute to adherence. All of the above considerations need to be discussed with the patient, and the patient should be empowered to participate in helping to choose the HAART regimen in order to optimize adherence.

There currently are eight approved agents that are nucleoside/nucleotide reverse transcriptase inhibitors (Table 1). Among these, four combination pills are currently available: zidovudine (AZT) plus lamivudine (3TC) plus abacavir (ABC), brand name Trizivir; AZT plus 3TC, brand name Combivir; emtricitabine (FTC) plus tenofovir disoproxil fumarate (TDF), brand name Truvada; and 3TC plus abacavir (ABC), brand name Epzicom. The latter

Year Introduced	Generic Name (abbreviation)	Brand Name
1987	zidovudine (ZDV,AZT)	Retrovir®
1991	didanosine (ddI)	Videx®
1992	zalcitabine (ddC)	Hivid®
1994	stavudine (d4T)	Zerit®
1995	lamivudine (3TC)	Epivir®
1997	zidovudine plus lamivudine (AZT plus 3TC)	Combivir®
1998	abacavir (ABC)	Ziagen®
2000	Zidovudine plus lamivudine plus abacavir (AZT plus 3TC plus ABC)	Trizivir®
2001	tenofovir disoproxil fumarate (TDF)*	Viread®
2003	emtricitabine (FTC)	Emtriva®
2004	emtricitabine plus tenofovir disoproxil fumarate (FTC plus TDF)	Truvada™
2004	lamivudine plus abacavir (3TC plus ABC)	Epzicom™

Table 1: Currently approved nucleoside and nucleotide reverse transcriptase inhibitors.

two fixed dose combinations were approved by the FDA on August 2, 2004. They both also have the potential advantage of being once daily medications.

The DHHS guidelines recommend (AZT or TDF) + (3TC or FTC) as the two agents in the NRTI backbone.<sup>1</sup> Alternatively, (stavudine (d4T) or didanosine (ddI) or ABC) + (3TC or FTC) can be used.<sup>1</sup> Both FTC plus TDF and 3TC plus ABC are two possible combinations that are part of either preferred or alternate regimens. The following addresses both combination pills with respect to adherence, tolerability, and resistance.

### Adherence

HAART regimens may be difficult to adhere to because of pill burden, dosing frequency, dosing schedule, food requirements, and side effects. Poor adherence significantly contributes to

## CASE STUDY: HAART TREATMENT

A case of a 22-year-old gay man who presented to our office with a diagnosis of HIV represents how the new combination pills can be used to create a regimen which is effective, easily tolerated and relatively simple for adherence. He was diagnosed 5 months prior in another state. He recently moved to New Jersey to live with extended family and has not been seen previously by an HIV physician. Blood work from our office revealed a repeatedly reactive HIV-1 antibody screen, and positive HIV-1 Western Blot.

His past medical history was significant only for viral meningitis. He has no drug allergies; his only current medication is a multivitamin. His risk factor for HIV was having unprotected sex with another man. His review of systems revealed fatigue, swollen lymph nodes in his neck, and anorexia.

On physical exam his temperature was 97.2°F, blood pressure 107/60, heart rate 59, and respirations 16. He stood 6'2" and weighed 200 pounds. His HEENT exam did not reveal thrush. His fundoscopic exam did not reveal cotton wool spots or retinal hemorrhages. He had small anterior and posterior cervical lymphadenopathy. His heart had a regular rate and rhythm, and his lungs were clear to auscultation. His abdomen was soft and nontender. His genitalia did not reveal lesions, penile discharge, or testicular masses.

Blood work revealed a CD4 count of 146 cells/mm<sup>3</sup>, and a viral load of >750,000 copies/ml. His screening labs were normal with the exception of a platelet count of 139,000/μl. His hepatitis A, B, and C serologies were non reactive.

During his initial visit, he was educated about HIV, safe sex, and adherence. The vaccination series for Hepatitis A and B was started, he was given a pneumococcal vaccination, and a PPD was placed. He was started on trimethoprim/sulfamethoxazole therapy for PCP prophylaxis. Finally, a HAART regimen was chosen consisting of FTC, TDF, and lopinavir/ritonavir. The side effects were discussed and he was given a prescription for the medications, but instructed not to start them until after returning to the office the following week for additional adherence counseling with a nurse.

I met with him two weeks after starting HAART and he had not experienced any side effects. He reported 100% adherence. Two weeks later, we met again to monitor his progress. At this time, the fixed dose combination pills were FDA approved, and his NRTI backbone was changed to FTC plus TDF. His CD4 count increased to 228 cells/mm<sup>3</sup> and his viral load was <400 copies/ml. Two months later he was tolerating his medications and reported good adherence; his CD4 count was 374 cells/mm<sup>3</sup> and viral load was 137 copies/ml. He continues to do well on this simple, easy to tolerate, and potent HAART regimen.

HAART failure. Paterson *et al.*<sup>4</sup> demonstrated that 22% of patients with adherence of 95% or greater had virologic failure, compared to 61% of patients with adherence of 80 to 95%. More recently, Sethi *et al.*<sup>5</sup> demonstrated that a cumulative adherence of 70 to 89% was independently associated with viral rebound and clinically significant resistance. These two studies show that extremely high adherence (>90 to 95%) is needed to lessen the development of drug resistance. Strategies to improve adherence include patient education, reminder strategies, enhanced side effect management, simplifying regimens, improving the patient-provider relationship, and optimizing psychosocial functioning. The two new fixed dose combinations are single pills that are taken daily. This can be a part of a simple regimen that may improve adherence by lowering pill burden and dose frequency.

### Tolerability

- 3TC plus ABC

Long-term experience with 3TC shows that it may have the fewest side effects among the NRTIs. Side effects may include diarrhea, malaise, fatigue, and headache. Class side effects warrant close monitoring when using the NRTIs. In general, mitochondrial toxicity and lipoatrophy occur less frequently with the use of 3TC compared to other NRTIs. Approximately 3% to 5% of patients taking ABC will develop a hypersensitivity reaction (HSR) within the first 6 weeks of ABC therapy. It is extremely important to alert patients of this possible adverse reaction prior to initiating therapy. The HSR consists of fever, rash, nausea, emesis, abdominal pain, malaise, fatigue, and headache. This syndrome needs to be differentiated from other adverse effects such as hepatotoxicity or mitochondrial toxicity, which also may occur early in the course of treatment. If a HSR is suspected then ABC should be stopped and the patient should not be rechallenged with the medications; fatalities have occurred.

- FTC plus TDF

The recently approved FTC has a tolerability profile that is similar to 3TC. It is extremely safe and well tolerated. A small percentage of patients may note hyperpigmentation of the palms and soles. Again, class side effects need to be kept in mind. TDF also is extremely well tolerated. Patients may develop gastrointestinal symptoms such as nausea, emesis, and diarrhea, but this has been similar to patients

receiving placebo. More concerning is the potential for worsening renal function in patients taking TDF. TDF is structurally similar to acyclic nucleosides didanosine and zalcitabine, which can cause nephrotoxicity. Several published clinical trials on the safety of TDF have demonstrated renal toxicity rates similar to placebo. However, case reports have been published that demonstrate TDF associated nephrotoxicity.<sup>6,7</sup> Accordingly, TDF should be used cautiously in patients with renal insufficiency.

- Resistance

Resistance can develop with both 3TC/ABC and FTC/TDF. There is no clear choice of which fixed dose combination medication to which resistance is preferred; obviously, it would be better not to develop any resistance at all. However, both agents contain either 3TC or FTC. These medications, along with other medications in their class, may cause the virus to develop the M184V mutation. This mutation confers resistance to both 3TC and FTC. Also, in combination with other mutations, the M184V mutation may cause resistance to other NRTIs. However, the M184V mutation increases susceptibility to AZT, d4T, and TDF. ABC can select for L74V which confers resistance to ABC and ddI. TDF can select for K65R. This mutation may confer resistance to TDF, and may result in resistance to ABC and ddI when other mutations are also present.

In summary, the DHHS has recently updated guidelines stating preferred and alternate HAART regimens, including recommending NRTI backbones.<sup>1</sup> FTC plus TDF and 3TC plus ABC are two newly FDA approved fixed dose combination medications that can be selected as a part of HAART therapy. Both agents are ideal for improving adherence because they are a single pill that is taken daily. As always, side effects and resistance issues need to be considered when choosing therapy.

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## INTERNET RESOURCES

### UMDNJ - CENTER FOR CONTINUING AND OUTREACH EDUCATION - DIVISION OF AIDS EDUCATION

[ccoe.umdj.edu/aids](http://ccoe.umdj.edu/aids)

Training programs for HIV/AIDS health and social service professionals. You can register online for most UMDNJ HIV/AIDS continuing education courses at:

[www.peopleware.net/o646a](http://www.peopleware.net/o646a)

Online CME at:

<http://ccoe.umdj.edu/online/index>

### NJDHSS-DHAS WEBSITE

[www.state.nj.us/health/aids/  
rapidtesting/index.shtml](http://www.state.nj.us/health/aids/rapidtesting/index.shtml)

New Jersey state rapid testing site! FAQs, locations, and articles.

[www.state.nj.us/health/aids/aidsprv.htm](http://www.state.nj.us/health/aids/aidsprv.htm)

Epidemiological reports, policies, and clinical guidelines for HIV/AIDS care and services in New Jersey. Free CME articles.

[www.state.nj.us/health/aids/aidsqtr.htm](http://www.state.nj.us/health/aids/aidsqtr.htm)

New Jersey HIV/AIDS Semi-annual Newsletter (statistical report).

### AETC NATIONAL RESOURCE CENTER

[www.aids-etc.org](http://www.aids-etc.org)

HIV treatment guidelines and key journal articles and news releases, links to all AIDS Education and Training Centers, training materials and curricula, and evaluation tools.

### AIDS INFO

[www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov)

A service of the US Department of Health and Human Services offering HIV/AIDS treatment guidelines, other information on prevention, treatment, and research.

# SAVE THE DATES!

New Jersey

**Thursday, April 21, 2005, 1:00- 3:00 PM:  
CDC Satellite Broadcast/Web Cast:**

## **Partner Counseling and Referral Services for HIV Prevention**

Viewing sites in Trenton and Newark. See  
website: [www.cdcnpin-broadcast.org/scripts/  
start.htm](http://www.cdcnpin-broadcast.org/scripts/start.htm)

Details TBA. Please contact Kimi Nakata with  
questions: (973) 972-1856

**Thursday, June 16, 2005: Iselin**

## **HIV Clinical Update 2005: New Jersey Statewide Conference**

Jointly sponsored by the UMDNJ Center for  
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Iselin, NJ: The Hilton Woodbridge

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National

**April 8-9, 2005: Dallas, TX**

## **2nd Annual Women & HIV Symposium:**

Texas/Oklahoma AIDS Education & Training Center  
and UMDNJ-CCOE-Division of AIDS Education  
jointly sponsor this state-of-the-art, evidence-  
based, multidisciplinary conference. Patricia M.  
Kloser, MD, MPH, Medical Director of the UMDNJ-  
CCOE-Division of AIDS Education, is the keynote  
speaker. See [www.aidseducation.org](http://www.aidseducation.org).

**April 10-13, 2005: Oakland, CA**

## **AmFAR 17th National HIV/AIDS Update Conference**

For information: American Foundation for AIDS  
Research: [www.amfar.org/nauc](http://www.amfar.org/nauc) or call (212) 806-  
1754.

**May 28-31, 2005: Chicago, IL**

## **HIV/AIDS 2005: "The Social Work Response: 17th Annual National Conference on Social Work and HIV/AIDS**

For more information call Boston College Graduate  
School of Social Work: 617-552-4038.

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