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HIV CLINICAL UPDATE
(see back cover)

New Jersey Department of Health and Senior Services Rapid HIV Testing Team Receives ASTHO Vision Award

Linda A. Berezny, RN, and Sindy M. Paul, MD, MPH, FACPM

The New Jersey Department of Health and Senior Services (NJDHSS) successful implementation of its rapid HIV testing program was honored with the Association of State and Territorial Health Officials (ASTHO) "Vision Award" at their 2006 Annual Meeting in Atlanta, Georgia. These awards honor outstanding state health department programs and initiatives. The awards provide peer recognition for creative state health programs and increase awareness of successful initiatives encouraging replication in other states.

New Jersey has a high prevalence of HIV/AIDS, ranking fifth in the nation for cumulative reported AIDS cases, third in the nation for cumulative reported pediatric AIDS cases, and has the highest proportion of AIDS cases in women. The Centers for Disease Control and Prevention (CDC) estimates that 250,000 persons infected with HIV in the United States do not know their HIV status.

The NJDHSS developed a program to provide rapid HIV testing at publicly funded counseling and testing sites. The goal is to increase the number of persons with identifiable risks who know their HIV/AIDS status. This initiative is consistent with Healthy People 2010 (HP2010) and Healthy New Jersey 2010 (HNJ2010). HP2010 includes a developmental objective: "Increase the Number of HIV Positive Persons Who Know Their Serostatus.[1]" In HNJ2010, there is a newly developed mid-course objective to: "Increase the Percentage of Persons Tested for HIV at Publicly Funded Sites Who Receive their Test Results.[2]"

The testing technology to provide rapid HIV testing as a point-of-care test became available in the United States in 2003. In November 2003, the first site for rapid HIV testing opened in New Jersey. Today there are over 160 sites in all 21 counties serving the people of New Jersey. The rapid HIV test is important to slowing the spread of HIV because it overcomes a major obstacle in HIV testing. Getting the results in 20 minutes means people no longer have to wait one or two weeks and return to the testing site to get their results.

NJDHSS rapid testing team: (left to right) Skip Drumm, Carmine Grasso, Linda Berezny, Susan Jacobs, Dr. Sindy Paul, Rhonda Williams, Maureen Wolski. Not pictured here: Laurence Ganges, Kenneth Earley, Aye Maung Maung, Lorhetta Nichol, Monica Talbert

In 2003, before rapid HIV testing was available, New Jersey's publicly funded counseling and testing sites performed 67,941 HIV tests. Of those, 23,230, or 34 percent never returned to the testing site for the results. With the rapid HIV test, clients receive their results 98.8 percent of the time.

Data for the first three years, from November 2003 to November 2006, indicate that 88,427 rapid HIV tests were performed at publicly funded counseling and testing sites. Of the persons tested, 87,392 (98.8%) received their results, 86,882 (98.3%) tested negative, 1,456 (1.7%) tested positive, and only 89 (0.01%) had a discordant result. Of the 1,456 persons testing positive, 1,011 (69.4%) were newly identified as being infected with HIV. Therefore, rapid HIV testing markedly increased the percentage of persons tested at publicly funded counseling and testing sites who received their results, and also a large proportion of those testing positive are newly diagnosed. This issue of AIDSLine highlights the successful expansion of the NJDHSS rapid HIV testing program to emergency departments.

Congratulations to the NJDHSS rapid testing team (pictured above).

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CONTINUING EDUCATION INFORMATION

HIV TREATMENT UPDATE

Release Date: March 1, 2007
Expiration Date: October 31, 2008
Course Code: 09HC03 - DE01

Sponsorship

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

Target Audience

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

Statement of Need

Antiretroviral therapy 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 drawback in use of earlier drugs have led to less common use. 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 adult and adolescents with HIV infections. The current guidelines include revised recommendations for treatment with evidence of resistance to 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.

REFERENCE: Department of Health and Human Services (DHHS). Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. October 10, 2006 http://aidsinfo.nih.gov

Learning Objectives

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

- Explain why some antiretroviral agent combinations are not recommended for use with most HIV patients.
- Describe the impact of the SMART trial on structured treatment interruptions.
- Discuss the primary causes of resistance to antiretroviral medication.

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.

Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a credit letter and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials. Estimated time to complete this activity as designed is 1.5 hours.

Accreditation

Physicians: UMDNJ–Center for Continuing and Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. UMDNJ–Center for Continuing & Outreach Education designates this educational activity for a maximum of 1.5 category 1 credits™ toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

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

This activity is awarded 1.5 contact hours.

UMDNJ-Center for Continuing and Outreach Education is an approved provider of continuing education by the California Board of Registered Nursing, Provider Number CEP 13780 for a maximum of 1.5 contact hours for this activity.

Review: 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 Patricia Kloser, MD, MPH. This activity was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Bonnie Abedini, RN, MSN; Mary C. Krug, RN, MSN, APN-C; and Debbie Y. Mohammed, MS, APRN-BC, ACRN.

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Stephen Smith, MD, 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.

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

Patricia Kloser, MD, MPH (Field Tester and Activity Director) has the following financial relationships to disclose: Speaker's Bureau: GlaxoSmithKline, Roche; Consultant: Gilead, Boehringer Ingleheim. The following have no financial relationships to disclose: faculty: Erin-Margaret Murphy, PA-C and Stephen Smith, MD; and field testers: Bonnie Abedini, BSN, MS; Mary C. Krug, RN, MSN, APN-C; and Debbie Y. Mohammed, MS, APRN-BC, ACRN.

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.

HIV TREATMENT UPDATE

Erin Margaret Murphy, PA-C, and Stephen M. Smith, MD
Saint Michael's Medical Center, Newark, NJ

LEARNING OBJECTIVES:

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

- *Explain why some antiretroviral agent combinations are preferred for use with HIV patients who are new to treatment.*
- *Describe the findings of the SMART trial on structured treatment interruptions.*
- *Discuss the primary causes of resistance to antiretroviral medication.*

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 necessary, produces revisions or updates. Since the first publication in 1998, 17 versions of the Guidelines have been released; the latest was published on-line at http://aidsinfo.nih.gov on October 10, 2006. Recommendations are based upon analysis of multiple trials and expert opinions. As the many versions of the Guidelines imply, HIV treatment changes very quickly. Drugs and approaches used just one year before are often replaced with newer, better therapies. HIV treatment providers use the Guidelines to improve their practice and to provide their patients with optimal care.

The goals of antiretroviral treatment, as summarized in the Guidelines, are to:

- REDUCE HIV-related morbidity and mortality,
- IMPROVE quality of life,
- RESTORE and PRESERVE immunologic function, and
- MAXIMALLY and durably SUPPRESS viral load.[1]

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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.

Section I: Overview of HIV Treatment Recommendations for the Treatment-Naïve Patient

Upon entering a clinic or private practice, each HIV+ patient should undergo an initial evaluation, with comprehensive physical examination and laboratory workup including CD4+ T cell count and viral load tests and often including genotypic resistance testing. Clinicians need to base treatment decisions on the findings of this evaluation, including history, symptoms, and laboratory results. Recommendations regarding this initial evaluation and decisions concerning initiation of treatment have not changed in the last two years.

The Guidelines recommend use of the following indications for initiation of antiretroviral therapy.[1]

- Antiretroviral therapy is recommended for all patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4+ T cell count.
- Antiretroviral therapy is also recommended for asymptomatic patients with <200 CD4+ T cells/mm^3, which is an AIDS-defining finding.
- Asymptomatic patients with CD4+ T cell counts of 201-350 cells/mm^3 should be offered treatment.
- For asymptomatic patients with CD4+ T cell of >350 cells/mm^3 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+ T cell counts of >350 cells /mm^3 and plasma HIV RNA <100,000 copies/mL.

The current indications for treatment are based on clinical data and observational cohorts that have not been recently challenged. Infectious disease specialists concur, based on many randomized clinical trials, that when the CD4+ T cell count is <200 cells/mm^3, there is a strong correlation with disease progression. For asymptomatic patients with a CD4+ T cell count >200 cells/mm^3, the Guidelines recommend that clinicians take into consideration other factors such as patient readiness and potential drug toxicities. However, most clinicians choose when to begin treatment based on the findings of clinical trials and observational data of untreated individuals with regular CD4+ T cell and HIV RNA level measurements.

The plasma HIV RNA level cut-off for starting treatment of an asymptomatic patient with a CDE+T cell count above 350 cells/mm^3 was raised to >100,000 copies/ml in the October 2004 Guidelines, due to the ART Cohort Collaboration study, which included 13 studies from Europe and North America. This study 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.

SELECTING AN ANTIRETROVIRAL REGIMEN

For patients who are naïve to HIV therapy, the Panel recommends selection of either an "NNRTI-based regimen" or a "PI-based regimen," that is, a regimen that is based on either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI),

TABLE 1. RECOMMENDED ANTIRETROVIRAL REGIMENS

Select 1 from Column A + 1 from Column B
(either NNRTI or PI) **(2-drug NRTI combination)**

	Column A	Column B
Preferred Combinations *(alphabetical order)*	**NNRTI** • Efavirenz[1] (Sustiva®) **PI** (boosted with ritonavir) • Atazanavir + ritonavir (Reyataz™ + Norvir®) • fosamprenavir + ritonavir BID (Lexiva™ + Norvir®) • lopinavir/ritonavir BID (Kaletra® + Norvir®	***2 NRTIs*** • tenofovir/emtricitabine[3] (Viread® + Emtriva™, combined as Truvada™) • zidovudine/lamivudine (AZT/Retrovir® + 3TC/Epivir®, combined as Combivir®)

	Column A	Column B
Alternative Combinations *(alphabetical order)*	**NNRTI** • Nevirapine[4] (Viramune®) **PI** • atazanavir (unboosted) (Reyataz™) • fosamprenavir (unboosted) (Lexiva™) • fosamprenavir + ritonavir (Lexiva™ + Norvir®) once daily • lopinavir/ritonavir (Kaletra®) once daily	***2 NRTIs*** • abacavir/lamivudine[3] (Ziagen® and Epivir®, combined as Epzicom®) • didanosine + emtricitabine (ddI or Videx® + Emtriva®) • didanosine +lamivudine (ddI or Videx® + Emtriva®

1 Efavirenz is not recommended for use in the 1st trimester of pregnancy or in sexually active women with child-bearing potential who are not using effective contraception.

2 The pivotal study that led to the recommendation of lopinavir/ritonavir as a preferred PI component was based on twice-daily dosing [106]. A smaller study has shown similar efficacy with once-daily dosing but also showed a higher incidence of moderate to severe diarrhea with the once-daily regimen (16% vs. 5%) [114].

3 Emtricitabine may be used in place of lamivudine and vice versa.

4 Nevirapine should not be initiated in women with CD4+ T cell count >250cells/mm3 or in men with CD4+ T cell count >400 cells/mm3 because of increased risk of symptomatic hepatic events in these patients.

5 Atazanavir must be boosted with ritonavir if used in combination with tenofovir.

Adapted from DHHS. 2006.[1]

combined with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs). There have been some changes with regards to patients who are naïve to HIV therapy.

However, the general recommendations remains the same regarding from which class of antiretroviral medications to choose from when constructing the patient's first regimen remain the same. The Panel classifies regimens as Preferred or Alternative and also recommends against the use of some medications (See Table 2).

As the preferred NNRTI based regimens, the Panel recommends efavirenz + (either tenofovir or zidovudine) + (either emtricitabine or lamivudine). An alternative NNRTI-based regimen is nevirapine + (either abacavir or didanosine) + (either emtricitabine or lamivudine). Efavirenz has a potential teratogenic effect, and thus caution should be used when prescribing it to women of child bearing age.

For PI-based regimens, the preferred initial protease inhibitors are, in alphabetical order, atazanavir boosted with ritonavir, fosamprenavir boosted with ritonavir, or lopinavir/ritonavir (co-formulated as Kaletra®). One of these PIs is then given with (tenofovir or zidovudine) + (emtricitabine or lamivudine). Alternative regimens are many and include a base of unboosted atazanavir, unboosted fosamprenavir, fosamprenaivr boosted with ritonavir once daily or Kaletra® once daily, combined with a 2-NRTI combination of (either abacavir or didanosine) + (either emtricitabine or lamivudine).

Clinicians are recommended to construct a regimen by choosing one component from Column A and one component from Column B as seen in the table. Currently available co-formulations play a large role in these recommendations. Clinicians have a range of preferences that may not always coincide with the DHHS Guidelines. For instance, the Guidelines recommend that tenofovir be given with emtricitabine, though some clinicians find no evidence that this combination is any more potent or better tolerated than tenofovir plus lamivudine. Zidovudine and lamivudine (co-formulated as Combivir) are still listed as a preferred NRTI combination. However, many clinicians, based in large part on the recent findings of the clinical trial Study 934, consider Combivir an alternative regimen.[2] On the other hand, clinicians familiar with abacavir and comfortable with managing the potential hypersensitivity reaction in the first six weeks of therapy may consider Epzicom (the co-formulation of abacavir and lamivudine) as another preferred NRTI combination.

Additional data have emerged, resulting in slight changes in the Guidelines. In 2006, two agents were added to the list of approved antiretroviral drugs available: tipranavir and darunavir. Both of these agents are in the Protease Inhibitor class and require boosting with ritonavir. These agents are discussed in more detail in the section on treatment-experienced patients. The FDA also approved a co-formulation of already approved agents tenofovir/emtricitabine/efavirenz into one pill, Atripla®. This marks the first multi-class one-pill-once-a-day regimen. Two antiretroviral agents have been dropped from the list, zalcitabine and amprenavir.

As with previous Guidelines, the Panel recommends against the use of some medications. Several options are considered acceptable as initial agents but inferior to the preferred or alternative components. These options include nelfinavir, ritonavir-boosted saquinavir, stavudine + lamivudine, and a triple-NRTI regimen containing abacavir + zidovudine + lamivudine. The following table from the Guidelines gives explanation of why these agents are considered inferior and specific circumstances for use.

(Continued on next page)

TABLE 2. ANTIRETROVIRAL REGIMENS THAT ARE NOT RECOMMENDED

Antiretroviral drugs or regimens *(in alphabetical order)*	Reasons for generally NOT RECOMMENDING the drugs or regimens as initial therapy	Special circumstances in which the drugs or regimens may be used
Abacavir/ lamivudine/ zidovudine (co-formulated) as triple-NRTI combination regimen	• Inferior virologic efficacy	• When PI or NNRTI-based regimens cannot be used based on toxicities or concerns of significant drug-drug interactions
Nelfinavir	• Inferior virologic efficacy	• Most experience with pregnant patients with good tolerability and adequate pharmacokinetic data
Saquinavir (ritonavir-boosted)	• Inferior to lopinavir/ritonavir • Minimal efficacy data in treatment naïve patients	• When preferred or alternative PI components cannot be used based on toxicities or concerns of significant drug-drug interactions
Stavudine + lamivudine	• Significant toxicities including lipoatrophy, peripheral neuropathy, hyperlactatemia including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis	• When preferred or alternative dual-NRTI combination cannot be used

Adapted from DHHS. 2006.[1]

Section II: Working with the Treatment-Experienced Patient

A. VIRAL RESISTANCE: DIAGNOSTICS AND STRATEGIES

Antiretroviral treatment regimens are designed to suppress HIV replication in actively replicating $CD4^+$ T cells. Although the Guidelines recommend three active agents from at least two different classes, the use of more than one active agent also reduces the risk of the virus mutating and developing resistance to one or more medications in the patient's current regimen. Patient adherence to the individually designed antiretroviral regimen is essential to the success of sustained virologic suppression. Some individuals have difficulty adhering to regimens for a variety of reasons including high pill burden, multiple doses per day, and adverse side effects. The consequence of non-adherence is viral resistance, which results in the elimination of available antiretroviral agents to use in future regimens. Other reasons for failure include sub-optimal pharmacokinetics (i.e. unsuspected drug-drug interactions), high baseline viral load, active substance abuse, and unknown reasons. Some controversy exists over when to change therapy and which new set of medications to select. Virologic, immunologic and/or clinical failures are all reasons to change therapy.

Virologic failure is the most common impetus for change of HAART. 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."* Studies have established that continuous administration of ART in the face of new and persistent viremia increases the number of drug resistance associated mutations. The more mutations that develop, the fewer drugs will remain active against a patient's virus.

When changing the drug regimen for treatment failure, the Panel recommends:

- For the patient with virologic failure, perform resistance testing while the patient is still taking the drug regimen or within 4 weeks after regimen discontinuation. Resistance testing may show falsely negative results otherwise, as the wild type virus re-populates after drug therapy is stopped.
- Use the treatment history and past and current resistance test results to identify active agents (preferably 3 or more) to design a new regimen.
- 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 agents).
- 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.

Resistance Testing

Genotypic and phenotypic testing will aid in the deciding of which is the best medication to be used when resistance is documented. It can be confusing to decide which test to use in different scenarios and there is no right answer. The genotype detects the mutations present in the relevant virus genes (Reverse Transcriptase, Protease, and Envelope), whereas the phenotype is an assay that measures the ability of HIV to infect a cell line at different concentrations of tested antiretroviral medications.

The phenotype assay tests the same genes listed above, but in a more biologic manner. In this assay, the viral genes, reverse transcriptase and protease, are first amplified via the polymerase chain reaction and then inserted in a recombinant provirus. The provirus is used to make single cycle virus, which is then used to infect a cell line in the presence of increasing amounts of an antiretroviral drug. Each FDA approved drug can be tested. The drug concentration, which decreases infectivity by 50% compared to the no-drug control, is called the IC50. The IC50 is then compared to that of wild type virus. Viruses with IC50's much greater than wild type are resistant. This information may be helpful in identifying a new regimen for a patient with treatment-resistant virus. However, phenotyping is much more expensive than genotyping, and the additional information is not always necessary.

Genotyping should always be done on the initial visit and/or prior to starting treatment for antiretroviral-naïve patients. When the clinician is suspecting failure secondary to NNRTI or NRTI resistance, a genotype gives sufficient information regarding the mutations to make a skilled and confident decision about the regimen switch. Also, the average cost of a genotype is approximately $450 and the approximate cost of the phenotype is $950. The phenotype becomes a more useful tool when the patient's regimen is more complicated and the clinician is suspecting more resistance to the PI class.

When deciding to switch regimens, the clinician has the choice of several recently approved treatment options. Tipranavir and darunavir are both Protease Inhibitors (PIs)

approved for use in patients with multiple resistance [see prescribing information]. These two agents have shown good activity in the face of multiple PI mutations. Tipranavir requires boosting with ritonavir 200 mg bid and thus is associated with a higher level of lipid abnormalities. Tipranavir also comes with two black box warnings: 1) intracranial hemorrhage and 2) clinical hepatitis and hepatic decompensation. Darunavir received accelerated FDA approval and is the most recently approved antiretroviral agent. Although darunavir is only approved for use in heavily treatment-experienced patients, it is currently being evaluated for use in less experienced patients.

Salvage therapy, for patients whose viral load is increasing despite antiretroviral treatment, most often needs to include these newer agents. However, some patients have either pre-existing resistance to these agents or have developed new resistance and have no current therapeutic options. In this setting it is of paramount importance to utilize the expanded access programs (EAPs) of heavily studied but not yet approved agents. There are currently two agents with EAPs available: TMC-125 (etravirine), which is a novel NNRTI, and MK-0518 which is the first in the new class of agents called Integrase Inhibitors. New classes of antiretroviral medications that target new or other viral proteins are crucial, given the efficacy of viral suppression when two steps or more of viral replication are blocked.

For patients who are either ineligible for EAPs or are in a holding regimen until another active agent becomes available, lamivudine or emtricitabine monotherapy has been shown to offer some efficacy.[4,5] Even in the face of the M184V mutation, which is the mutation selecting for lamivudine and emtricitabine, data reflects it is better to treat with either agent as monotherapy than to withhold all antiretroviral treatment.

B. TREATMENT INTERRUPTIONS: FINDINGS OF THE SMART TRIAL

With the advent of Highly Active Antiretroviral Therapy (HAART) there has been a great deal of success in achieving long term virologic suppression. However, there has been a considerable amount of interest in the efficacy and safety of structured treatment interruptions (STI). Continuous treatment with potent antiretroviral agents can lead to toxicities and resistance as well as being quite costly and demanding on the daily life of patients. Thus, strategies that involve cycles of treatment withdrawal and re-initiation were heavily studied in the past two years. Some of these studies looked at the intermittent approach, that is, pre-specified times of treatment withdrawal, and others focused on the CD4 cell count-guided approach. The largest and most recognized of these was the SMART trial.

The SMART trial commenced in 2001 and was designed to compare two antiretroviral treatment strategies, the drug conservation (DC) strategy and the viral suppression (VS) strategy.[3] The DC group planned to conserve treatments by deferring their use while the risk of opportunistic disease is low. This group stopped or deferred therapy until the CD4 cell count fell below 250 and would then use CD4 guided episodic treatment to increase CD4 to >350. The VS group aimed for sustained virologic suppression, irrespective of disease risk, and thus started treatment to maintain suppression irrespective of CD4 cell count. The trial enrolled 5,472 HIV infected subjects with a CD4 cell count of at least 350 who were then randomized 1:1 to each group.

The SMART trial halted enrollment early, due to the higher rates of death and HIV disease progression in the DC group. Unexpectedly, patients in this episodic treatment group also had a higher incidence of adverse events such as cardiovascular events, renal disease, liver disease and other end organ damage than those in the VS group. Experts were surprised by these results, given the notion that antiretroviral agents are associated with metabolic complications such as lipid abnormalities and decreased kidney and liver function. More importantly, patients in the DC group had a significantly higher mortality rate.

Subsequently, based on the SMART study design, it can be concluded that episodic use of antiretroviral therapy based on CD4 cell count levels is inferior to continuous antiretroviral therapy for management of the treatment-experienced patient.[3]

The results of the SMART trial and other STI studies have not made their way into changes in the Guidelines, but they definitely have clinical implications to be noted. Most of the data is leaning towards the conclusion that treatment interruption is not a good strategy and should be used only with great caution. The rebound viremia associated with treatment interruption has caused serious related adverse events. The data suggests that HAART should be continued once it is started, to reduce these adverse events.

Although the SMART and other STI trials did not examine this issue in any way, their results have prompted many to re-explore the recommendations for treatment initiation. In the SMART trial, DC group patients with baseline CD4 cell counts above 650 still had a significantly higher death rate and increased HIV disease progression. This subgroup analysis suggests that earlier treatment initiation may in fact be beneficial, especially with the newer, better-tolerated HIV therapies. The debate on when to initiate treatment is ongoing, and the STI trials imply that further clinical research on this topic is still needed.

(Continued on next page)

Section III: Co-Morbidities and Polypharmacy

With the success of HAART, ongoing drug development, clinical research and a general improved understanding of how to best treat the HIV+ patient, patients are living much longer than previously. This leaves the door open for patients to experience multiple co-morbidities, some of them because of or exacerbated by the HIV and some occurring completely independently. Regardless of the cause, the clinician must take into consideration the polypharmacy and consequential drug interactions that are most likely taking place. It is nearly impossible to know all potential drug interactions with the HIV medications as well as medications often prescribed for HIV-related illnesses. Therefore, it is important to know the most common ones and where to easily access information about the others. It is quite common for patients to utilize several different physicians, thus increasing the number of prescribers. For this reason, it is of vital importance to take a detailed history of all active medications during the initial visit and to question patients about any new medications, which may include over-the-counter and herbal preparations, at each follow up visit.

One of the most frequently missed drug interactions is with methadone. This is because the use of methadone is tightly restricted and can only be prescribed and distributed at authorized methadone clinics. Intravenous drug use represents the second most common risk factor for HIV transmission, therefore representing a large portion of the HIV+ population. The use of methadone as treatment for heroin or opiate addiction is controversial but widely used. When used properly, methadone has been shown to reduce drug use and related disease among heroin users. However, methadone comes with a variety of challenges to HIV treatment. If not used properly, methadone has the potential to be abused and heighten the level of other addictive agents in the body. In addition, methadone has multiple interactions with antiretroviral medications. Methadone decreases the levels of stavudine, but no dose adjustment is necessary. Methadone dose adjustment may be necessary in the following antiretrovirals, as they decrease the level of methadone in the body: efavirenz, nevirapine, ritonavir, fosamprenavir, nelfinavir, and lopinavir/ritonavir.

Another commonly prescribed class of medication is proton pump inhibitors (PPIs). PPIs have been shown to reduce the level of atazanavir, a commonly used protease inhibitor. Additionally, medications are often prescribed to help reduce cholesterol, which may be elevated in HIV positive patients. The blood levels of certain statins are increased when prescribed with protease inhibitors. Therefore, simvastatin and lovastatin are contraindicated, and caution should be used when prescribing atorvastatin and fluvastatin. A more recently released statin, rosuvastatin, appears to have less interaction with ritonavir and may be safer.[6] However, caution should be maintained when using a statin and ritonavir administered together. Also, tenofovir, the only nucleotide reverse transcriptase inhibitor, has nephrotoxic potential. The prescriber must take note of pre-existing renal dysfunction as well as whether any provider is co-prescribing other potentially nephrotoxic agents.

Conclusion:

The Guidelines provide invaluable information and offer recommendations to clinicians who care for HIV+ patients. The treatment recommendations are based on clinical studies and the relevant references are listed at the conclusion of this article. The recent changes to the Guidelines serve as subtle reminders of the ever-changing arena of HIV treatment. Seasoned specialists may have already adopted these changes, but primary care clinicians should review them periodically to gain expert advice from the literature and from those who treat HIV exclusively. The breadth and length (115 pages) of the Guidelines reinforce to the reader that the treatment and management of HIV is the most complicated medical treatment, bar none.

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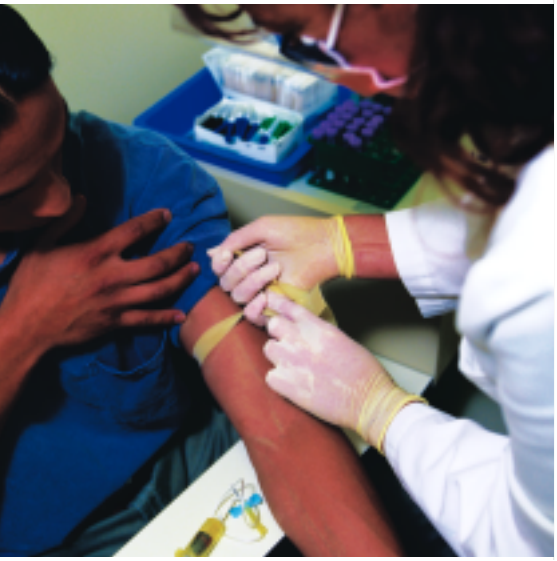
Case Scenarios

CASE SCENARIO #1:

A 45 year-old man presents to your practice for treatment after being recently being diagnosed as HIV-positive. 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 $CD4^+$ T-cell count and viral load are 482 cells/mm^3 and 88,632 copies/ml respectively.

Does this patient require anti-retroviral therapy?

Answer: No. His $CD4^+$ T-cell count is >350 cells/mm^3 and his viral load is <100,000 copies/ml. Therefore, according to the current Guidelines, he should have his $CD4^+$ T-cell count and viral load measured every 3-4 months. If his viral load increases to >100,000 copies/ml or when his $CD4^+$ T-cell count falls to <350 cells/mm^3, then he should be offered therapy. This patient's $CD4^+$ T-cell count will decrease by an estimated 60-80 cells/mm^3 per year. However, therapy will be just as effective if it is delayed until then.



CASE SCENARIO #2:

A 29 year-old woman is admitted to the hospital for fatigue, night sweats and weight loss and is diagnosed with Mycobacterium avium complex infection and HIV. She is referred to you after her discharge from the hospital. The patient has no other medical problems. She expresses a desire to become pregnant. Baseline labs show that her viral load is 68,000 copies/ml and her $CD4^+$ T-cell count is 71 cells/mm^3.

Should this patient be offered therapy?

Answer: Yes. Her $CD4^+$ T-cell count is <200 cells/mm^3 and she has had an AIDS defining illness therefore antiretroviral therapy is indicated.

Which regimen should she be offered?

Answer: The patient expresses a desire to become pregnant, therefore efavirenz should be avoided. Nevirapine is associated with increased liver toxicity in women with $CD4^+$ T-cell count >250 cells/mm^3. *However, this is a possible choice for this patient, as her CD4 count is only 71 cells, and Nevirapine has been used in pregnant women to prevent the transmission of HIV disease to unborn infants.* A PI-based regimen is a good choice, if the patient may become pregnant. A ritonavir-boosted-PI based regimen may be used.

CASE SCENARIO #3:

An HIV^+ 45 year-old male comes to your clinic after being out of care for several years. He has been on multiple anti-retroviral medications in the past but he is unable to recall specific names. He has a long history of uncontrolled hypertension but denies any other medical problems. He denies recreation drug use. His baseline labs show that his viral load is 354,000 copies/ml and his $CD4^+$ T-cell count is 189 cells/mm^3 as well as a genotype with multiple mutations in both the NRTI and PI classes.

Should this patient be offered therapy?

Answer: Yes. His $CD4^+$ T-cell count is <200 cells/mm^3 and his viral load is >100,000 copies/ml.

Which regimen should he be offered?

Answer: This patient would benefit from a phenotype. Based on the PI mutations present he could possibly benefit from one of the PIs indicated for heavily treatment-experienced patients. Otherwise he might be a suitable candidate for referral to an infectious disease clinical research program for Expanded Access to drugs which are not yet FDA approved.

INFORMATION RESOURCES

FDA MedWatch
Updated reports on medication interactions and warnings:
1-800-FDA-1088; Subscribe to e-bulletin: http://www.fda.gov/medwatch/elist.htm

Stanford resistance database:
Clinical Trials datasets, Summaries of Clinical Studies, Antiretroviral drug summaries, Query function for analysis of genotype data. http://hivdb.stanford.edu

CE

SELF-ASSESSMENT TEST

HIV TREATMENT UPDATE

Self-Assessment Test

Questions refer to the content of the article and the notes that follow. To receive CME/CEU credit: complete exam, registration, and evaluation forms on-line at http://ccoe.umdnj.edu/online/AIDSLine/index.htm or fill in the forms on the next two (2) pages, and mail or fax to UMDNJ-CCOE (see next page).

1. **For an HIV-positive patient with no HIV-related symptoms (asymptomatic) and CD4$^+$ T-cell count of 201-350 cells/mm^3, the DHSS Guidelines always recommend**
   a. Antiretroviral therapy should be offered to patient.
   b. No antiretroviral therapy; monitoring only.
   c. Assessment for possible need for antiretroviral therapy.
   d. Not applicable: treatment not required unless patient is symptomatic.

2. **The ART Cohort Collaboration study showed that clinical progression was associated with a viral load of:**
   a. >55,000 copies/ml.
   b. >75,000 copies/ml.
   c. >100,000 copies/ml.
   d. No level has been established.

3. **According to the data from the SMART trial, interruptions in antiretroviral treatment based on CD4 levels are an acceptable treatment option for treatment-experienced patients.**
   a. True.
   b. False.

4. **The following NNRTI should be used with caution for women who are pregnant or of childbearing age:**
   a. Delavirdine.
   b. Nevirapine.
   c. Efavirenz.
   d. None of the above.

5. **Reasons for virologic failure include:**
   a. Drug-drug interactions.
   b. Incomplete drug adherence.
   c. a and b.
   d. None of the above.

6. **Phenotyping is typically used in:**
   a. ARV-treatment naïve patients.
   b. Patients who are failing an NRTI-based regimen.
   c. Patients who are failing a PI-based regimen.
   d. All of the above.

7. **Expanded Access Programs for nearly approved antiretroviral medications can be utilized optimally for which patient population?**
   a. Highly treatment-experienced who have few to no options.
   b. ARV-treatment naïve patients.
   c. Patients who are virologically suppressed on their current treatment regimen.
   d. None of the above.

8. **The newly approved agents included in the latest version of the guidelines, tipranavir and darunavir, are currently appropriate for use in the following patient population:**
   a. PI naïve patients.
   b. ARV-treatment naïve patients.
   c. Patients possessing PI resistance.
   d. All of the above.

9. **Methadone reduces the level of which antiretroviral medication?**
   a. Efavirenz.
   b. Lamivudine.
   c. Nelfinavir.
   d. None of the above.

10. **Which drug interacts with proton pump inhibitors?**
    a. Abacavir.
    b. Efavirenz.
    c. Atazanavir.
    d. Enfuvirtide.

CE Activity Code 09HC03 - DE01

CONTINUING EDUCATION REGISTRATION

HIV TREATMENT UPDATE

Registration Form

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In order to obtain continuing education 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 next page, and record your test answers below.

(3) Send the registration and evaluation forms to: UMDNJ-Center for Continuing and Outreach Education
• VIA MAIL: PO Box 1709, Newark, NJ 07101-1709 • VIA FAX: (973) 972-7128

(4) Retain a copy of your test answers. Your answer sheet will be graded and if you achieve a passing score of 70% or more, a credit letter awarding 1 AMA/PRA category 1 credit™ or 1.0 continuing education units, and the test answer key will be mailed to you within four (4) weeks.

Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again. This activity will be posted online at http://ccoe.umdnj.edu/catalog/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.*	**1.** A B C D	**3.** A B	**5.** A B C D	**7.** A BC D	***9.*** A B C D
	2. A B C D	**4.** A B C D	**6.** A B C D	**8.** A B C D	**10.** A B C D

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CONTINUING EDUCATION EVALUATION

HIV TREATMENT UPDATE

Activity Evaluation Form

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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 completed evaluation form.

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:		**Strongly Agree**				**Strongly Disagree**
Objective 1:	Explain why some antiretroviral agent combinations are not recommended for use with most HIV patients.	5	4	3	2	1
Objective 2:	Describe the impact of the SMART trial on structured treatment interruptions.	5	4	3	2	1
Objective 3:	Discuss the primary causes of resistance to antiretroviral medication.	5	4	3	2	1

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

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

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

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Contraindicated Medications and Regimens for HIV Infected Patients

John J. Faragon, Pharm.D.

LEARNING OBJECTIVES:

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

1. *List and describe mechanisms for drug-drug interactions considered contraindicated with HIV medications.*
2. *Identify HIV medications and/or regimens that should not be offered to patients at any time due to toxicity issues or due to poor response.*
3. *Classify antiretroviral regimens as preferred, alternative, or not recommended.*

Introduction

The use of highly active antiretroviral therapy (HAART) has resulted in dramatic reductions in morbidity and mortality for patients infected with HIV.[1] Current guidelines for the use of initial antiretroviral (ARV) therapy reflect the multitude of clinical trial data that have helped to shape the appropriate treatment of HIV infection.[2] Despite the widespread availability of the guidelines in print and web format, contraindicated regimens may still be used by providers. This article will address regimens and combinations to be avoided in HIV treatment.

HIV medical care providers must constantly update their knowledge of current medication guidelines, based on the findings of patients taking these medications in clinical trials and once they have been released on the market. The New Jersey Department of Health and Senior Services (NJDHSS), through the AIDS Drug Distribution Program (ADDP) conducts periodic reviews of prescription patterns to identify errors and patterns of prescribing suboptimal combinations. In 2002, NJDHSS became aware that some providers were prescribing combinations including: stavudine + zidovudine; invirase + 2 nucleoside analog reverse transcriptase inhibitors (NRTIs); zalcitabine + didanosine; zalcitabine + stavudine; and zalcitabine + lamivudine.[3] According to Sindy Paul, MD, MPH, Medical Director for the NJDHSS Division of HIV/AIDS Services (written communication, January 2007), NJDHSS and ADDP responded to this finding by initiating a system of "hard edits" that require the pharmacist to contact the prescribing provider to clarify the regimen, to minimize the risk of a patient receiving a contraindicated combination of antiretroviral agents.

We recommend that clinicians and pharmacists read this article for a summary of recommended and contraindicated regimens, and refer to the most recent DHHS antiretroviral treatment guidelines online at www.aidsinfo.nih.gov. In addition, a free continuing medical education lecture on diagnosis and management of HIV disease funded by NJDHSS, is available through the UMDNJ-Center for Continuing and Outreach Education (see page 23).

Preferred Regimens in DHHS Guidelines

The DHHS Guidelines were recently updated in October 2006, expanding the list of preferred antiretroviral therapy regimens.[2] For providers initiating patients on a non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimen, the preferred NNRTI is efavirenz, in combination with either zidovudine/lamivudine or tenofovir/emtricitiabine. When initiating therapy with a protease inhibitor (PI) based regimen, the ritonavir boosted protease inhibitors atazanavir/ritonavir, fosamprenavir/ritonavir, or lopinavir/ritonavir, in combination with either zidovudine/lamivudine or tenofovir/emtricitabine are preferred.

We recommend that clinicians and pharmacists read this article for a summary of recommended and contraindicated regimens, and refer to the most recent DHHS antiretro-viral treatment guidelines online at www.aidsinfo.nih.gov

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ARV Regimens/Components Not to be Offered at ANY Time

Amprenavir liquid in pregnancy, children <4 years old, patients with renal and/or hepatic dysfunction, patients treated with disulfiram or metronidazole or in combination with ritonavir liquid

Although amprenavir capsules were recently taken off the market, the solution is still available from the manufacturer. Due to the large amount of propylene glycol in the formulation, it should not be used in the following patients: women who are pregnant, children less than four years old, and in those with renal or hepatic dysfunction. The propylene glycol in the liquid formulation may accumulate, leading to glycol toxicity in these patient populations. Patients may also experience an antibuse-like reaction when combining the amprenavir liquid with disulfiram or metronidazole. Large amounts of ethanol in the ritonavir liquid formulation may also accumulate in patients receiving amprenavir and ritonvair liquids concurrently.[2]

Atazanavir and Indinavir

The protease inhibitors atazanavir and indinavir are both associated with the development of hyperbilirubinemia. Concurrent use of these medications has the potential to cause additive increases in bilirubin levels, and they should not be used together.

Didanosine and Stavudine

Didanosine and stavudine were commonly used in many of our combination regimens in the mid to late 1990s. However, our understanding of the toxicities of these medications has led to recommendations that concurrent use of didanosine and stavudine in any ARV regimen be avoided. Both stavudine and didanosine have been associated with peripheral neuropathy, pancreatitis and hyperlactatemia.[4,5] Their use together should be avoided because of the risk of overlapping toxicities. In pregnant women, concurrent stavudine and didanosine has been associated with reports of serious, even fatal cases of lactic acidosis and hepatic steatosis.[6] Providers should avoid this combination in HIV infected pregnant patients.

Efavirenz in 1st trimester of pregnancy or in women of significant child bearing potential

Efavirenz has been shown to be teratogenic in nonhuman primates and is classified as Pregnancy Category D.[7,8] In patients who are pregnant or of significant child bearing potential, including those who are unreliable in using barrier contraception, efavirenz should be avoided. For women who are pregnant, recent updates to the DHHS Guidelines for ARV use in pregnancy recommend either lopinavir/ritonavir, nelfinavir, or nevirapine, in combination with zidovudine/lamivudine.[9] Though the DHHS guidelines do not include saquinavir in pregnancy, the IAS guidelines do include this agent as an acceptable medication to be used in pregnancy. Current IAS guidelines are posted at http://www.iasusa.org/pub/arv_2006.pdf

Emtricitabine and lamivudine

Emtricitabine and lamivudine are both cytosine analogues and therefore should not be used together due to the risk of antagonistic interactions.

Monotherapy or Dual Therapy with NRTI or NNRTI

Due to the potential for rapid development of HIV resistance and inferior virologic efficacy, patients should NOT be receiving monotherapy with NRTIs or NNRTIs.[2] Though data has been presented on the use of lopinavir/ritonavir and atazanavir/ritonavir as monotherapy, use of these medications alone is still considered investigational and should not be done without close observation or in the setting of a clinical trial.[10,11] Despite guideline recommendations to avoid monotherapy, one rare, controversial exception is the use of zidovudine for the prevention of perinatal HIV transmission.[9,12]

Dual nucleoside regimens (ie: zidovudine/lamivudine, Combivir®, alone) should be avoided due to the risk of virologic failure and the likelihood of rapid development of resistance. Therefore, patients should be receiving the preferred triple drug regimens.

Nevirapine in treatment naïve women with CD4>250 or in men with CD4>400

Nevirapine therapy has been associated with symptomatic (and even fatal) hepatoxicity.[13] Data demonstrates that hepatotoxicity is more likely to occur in ARV-naïve women with CD4 counts >250 or in ARV-naïve men with CD4 counts greater than 400.[14] Patients may also experience skin rashes, fever and flu like symptoms in the setting of hepatotoxicity. In rare cases, hepatotoxicity may continue to evolve even after discontinuation of the medication. Therefore, nevirapine should only be used within the recommended CD4 parameters with routine monitoring of hepatic function, unless the benefit outweighs the risk.

Saquinavir as the sole Protease inhibitor

The protease inhibitor saquinavir was previously available in two formulations; Fortovase® (soft gelatin capsules) and Invirase (hard gel capsule). Pharmacokinetic data supported that when patients were receiving ritonavir boosted Invirase®, they were less likely to experience gastrointestinal side effects and saquinavir drug levels were improved when compared to ritonavir boosted Fortovase®.[15] As a result, Fortovase® was recently removed from the market and Invirase® was reformulated into a tablet formulation, reducing overall pill burdens for saquinavir based regimens. However, when saquinavir is used alone without ritonavir boosting, its drug levels are likely to be inadequate for the effective treatment of HIV infection. As a result, current guidelines do not recommend using Invirase® alone as the sole PI. Patients receiving saquinavir should also be receiving low dose ritonavir in addition to NRTIs.

Triple NRTI Regimens (except abacavir/zidovudine/lamivudine, and possibly tenofovir/zidovudine/lamivudine)

Triple NRTI regimens were initially studied in HIV infection due to their relatively low pill burdens, potential for once daily dosing, and to avoid toxicity for PI or NNRTI based regimens. However, clinical trial data in recent years has demonstrated that the triple NRTI regimens do not perform as well as standard NNRTI or PI based regimens. As an example, the triple NRTI regimens abacavir/tenofovir/lamivudine and tenofovir/didanosine/lamivudine (both once daily regimens with low pill burden) were associated with early, virologic failure when used in ARV-naïve patients; patients who failed this regimen were also likely to develop significant NRTI resistance.[16,17] As a result, triple NRTI regimens, alone, should not be used in patients with HIV infection.

One potential exception is the use of the twice daily triple combination of abacavir/zidovudine/lamivudine (Trizivir®). However, in the ACTG 5095, abacavir/zidovudine/lamivudine was shown to be inferior to both efavirenz + abacavir/zidovudine/lamivudine AND efavirenz + zidovudine/lamivudine.[17] As a result of this study, both the DHHS and the IAS-USA Guidelines removed abacavir/zidovudine/lamivudine from the preferred list of initial treatment regimens.[2,18] Therefore, the use of abacavir/zidovudine/lamivudine, alone, should be avoided unless a PI or NNRTI cannot be used due to toxicities or concerns for significant drug interactions, as this regimen is considered inferior to preferred regimens.[2] Though no data supports its use, tenofovir/zidovudine/lamivudine may also be an acceptable regimen.

Stavudine and Zidovudine

Stavudine and zidovudine should never be combined. Since zidovudine and stavudine are both thymidine analogues, they can compete for the same phosphorylation site in the growing chain of HIV DNA, resulting in an antagonistic, pharmacodynamic interaction. Thus, guidelines do not recommend their co-administration at any time.[2]

Zalcitabine and Stavudine or Zalcitabine and didanosine

The concomitant use of zalcitabine (ddC or dideoxycytidine) with drugs that have the potential to cause peripheral neuropathy, e.g., Stavudine or didanosine, should be avoided, because of overlapping neurotoxicity. As noted in Table 2, zalcitabine plus stavudine is contraindicated due to additive peripheral neuropathy.

ARV Regimens/Components Not To Be Offered in INITIAL ARV Regimens

Darunavir with ritonavir

Darunavir cannot be recommended to be used in initial treatment regimens since available data on this medication to date have been in ARV-experienced patients. Though current guidelines do not recommend the use of darunavir in initial treatment regimens, clinical trials are underway to determine its role in earlier lines of therapy.[20]

Delavirdine

The NNRTI delavirdine should not be used in initial treatment regimens due to its inferior virologic efficacy in relation to other preferred initial regimens. Delavirdine is also dosed two to three times daily with a relatively large pill burden. Therefore, delavirdine is not recommended to be used in initial treatment regimens.

Didanosine +Tenofovir

The use of didanosine and tenofovir as a nucleoside backbone should not be use in initial ARV regimens. This recommendation is based on clinical trial data in ARV-naïve subjects that demonstrated inferior virologic efficacy when didanosine and tenofovir was combined with efavirenz.[21] Studies also have shown that when this combination is used, increases in CD4 cell counts are often blunted.[22] As a result, this combination should not be offered in initial treatment regimens.

Enfuvirtide

Due to the lack of data in treatment naïve patients, the use of injectable enfuvirtide should be reserved for experienced patients in combination with at least two other new agents.

Indinavir (Unboosted or Ritonavir Boosted)

Unboosted indinavir should be avoided in ARV-naïve subjects for several reasons: it needs to be taken on an empty stomach, requires administration every eight hours, and requires patients to consume 1.5 liters of water daily. Though ritonavir boosted indinavir can be taken twice daily, there is an increased risk of nephrolithiasis compared to unboosted indinavir in patients receiving this regimen.

Ritonavir as the Sole Protease Inhibitor

Ritonavir as the sole protease inhibitor is dosed at 600 mg (6 X 100 mg capsules) twice daily. Gastrointestinal intolerance including diarrhea and nausea limit its use in initial treatment regimens. Lower doses of 100-200 mg one to two times daily are frequently used in combination with other protease inhibitors (with the exception of nelfinavir) to provide a pharmacokinetic boost which enhances drug levels. High dose ritonavir as the sole PI should be avoided in patients initiating therapy.

Tipranavir

Tipranavir should also not be used in initial treatment regimens, as the majority of data on this medication are in experienced patients. In addition, two black box warnings, one regarding the risk of hepatotoxicity and one for rare cases of fatal and non-fatal intracranial hemorrhages limit its use.[2]

Combinations to Avoid Due to Drug Drug Interactions

HAART is often complicated by drug-drug and drug herbal interactions. In particular, the NNRTIs and the PIs are often most problematic since these drugs are extensively metabolized by CYP450 enzyme system. A more extensive overview of drug interactions can be found elsewhere, however, this section will review interactions which should be not be used with patients on ARV therapy. [2, 22]

Antimycobacterial Medications

Concurrent tuberculosis and HIV presents the clinician with numerous challenges, including potential drug-drug interactions. The antimycobacterial medication rifampin or rifapentine is often used as part of an initial 4 drug regimen to treat tuberculosis in HIV infection.[24] However, due to its CYP450 induction properties, it is likely to significantly reduce the drug levels of the protease inhibitors by approximately 80-90%, even if they are boosted with low dose ritonavir.[25] This can place patients at significant risk for virologic failure and or drug resistance. As a potential option, providers may be able to select an efavirenz based regimen. For example, efavirenz can be used concurrently with rifampin, preferably with efavirenz 800mg.[2] However, in patients weighing less than an 50kg, standard efavirenz dosing of 600mg may be acceptable.[2] Nevirapine levels may be reduced by 20%-58% and therefore concurrent use with rifampin is not recommended. In patients requiring rifamycin therapy and receiving concurrent protease inhibitor based therapy, the use of rifabutin is recommended as an alternative; current guidelines for rifabutin and protease inhibitor therapy can be found elsewhere.[26]

Ergot Alkaloids

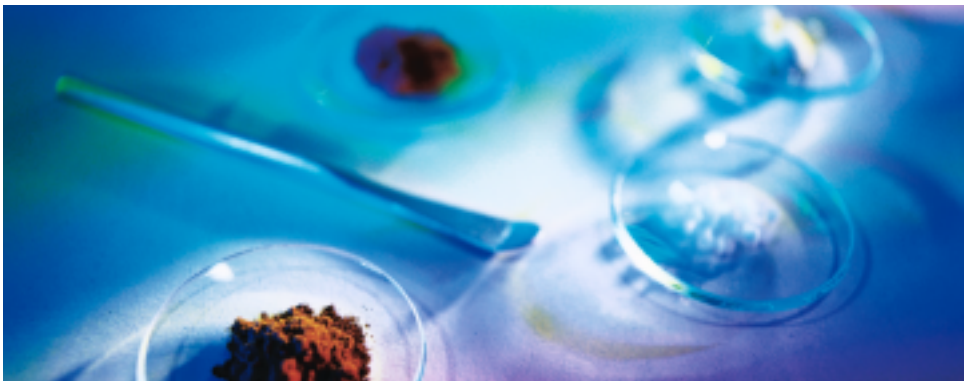
Fatal and non-fatal cases of ergotism have been reported when protease inhibitors are co-administered with ergot alkaloids.[27,28] Therefore, ergot alkaloids such as dihydroer gotamine, methylergonavine, and ergonaive should always be avoided in patients receiving PI or NNRTI based regimens.

Fluticasone

Inhaled fluticasone has been associated with Cushing's syndrome and adrenal insufficiency in patients receiving concurrent ritonavir-boosted protease inhibitors.[29,30] As a result, this combination should be avoided. This interaction is thought to be mediated through CYP450 inhibition from the ritonavir boosted protease inhibitors ability to increase fluticasone levels (which is also metabolized by CYP450). A potential alternative to fluticasone is beclomethasone.

Lipid Lowering Medications

Hyperlipidemia is a common problem with HIV treatment, especially with ritonavir boosted protease inhibitor regimens. As a result, treatment for hyperlipidemia is often warranted. The HMG-CoA Reductase Inhibitors (statins) are commonly used to treat hyperlipidemia. However, some of the drugs in the statin class are contraindicated since they are extensively metabolized by CYP3A4, similar to the protease inhibitors. For example, lovastatin and simvastatin are contraindicated with the PIs and the NNRTI delavirdine.[31] Statins least likely to cause significant interactions are pravastatin, except with darunavir, or low dose atorvastatin or low dose rosuvastatin.[2]



Proton Pump Inhibitors and Histamine 2 Receptor Antagonists

The concurrent use of the proton pump inhibitors and atazanavir are associated with significant reductions in atazanavir concentrations.[32] Therefore, all proton pump inhibitors (such as omeprazole, lansoprazole, esomprazole, rabepraolze) are not recommended to be taken with concurrent atazanavir therapy. Proton pump inhibitors should also be avoided in patients receiving the NNRTI delavirdine as well. Other protease inhibitors such as darunavir, fosamprenavir, lopinavir/ritonavir and saquinavir are unlikely to result in significant reductions in protease inhibitor drug levels.

Psychotropics/Neuroleptics

Midazolam and triazolam are contraindicated with PI or NNRTI therapy. Concurrent use will likely increase the drug levels of midazolam and triazolam significantly, resulting in increased sedation. Therefore these medications should be avoided and alternatives selected. Similarly, the neuroleptic medication pimozide should also be avoided in patients receiving protease inhibitor therapy.[2]

St. John's Wort

The use of St. John's Wort is contraindicated in patients receiving PI or NNRTI therapy.[2] Studies with indinavir and St. John's Wort demonstrated over a 50% reduction in indinavir concentrations.[33] Therefore, providers are encouraged to question patients regarding the use of herbal therapy and ensure that patients are aware that some herbal therapies may reduce levels of their HIV medications. Similar data has also been reported with garlic supplementation. [34]

Conclusions

The DHHS Guidelines have been recently updated to include regimens which are appropriate for patients and regimens to be avoided in HIV infection. This overview provides a summary of what should be avoided in HIV infected patients, based upon the current treatment guidelines. In avoiding medications and regimens that should not be used in HIV infection, we will likely improve the care of patients with HIV infection and continue to decrease morbidity and mortality for our patients.

CONTRAINDICATED MEDICATIONS AND REGIMENS FOR HIV-INFECTED PATIENTS

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CASE SCENARIO #1:

A 38 year old, African American, female patient is receiving ritonavir boosted lopinavir, tenovofir, and emtricitabine. Despite undetectable viral load and stable CD4 counts, the patients lipids are elevated.

What statin medication should not be coadministered with this patient's ARV regimen?

Answer: Both simvastatin and lovastatin are contraindicated with PI based regimens. As an alternative, low dose atorvastatin, low dose rosuvastatin, or pravastatin would be acceptable options. Even when using these drugs, it is important to monitor for signs of statin toxicity such as myaligias, CPK elevations, and LFT increases.

CASE SCENARIO #2:

A 31 year-old man is admitted to the hospital for acute pancreatitis and lactic acidosis. His ARV regimen includes Nelfinavir, stavudine, and didanosine. This is his first ARV regimen and he reports that he is "undetectable" (viral load).

Which medication is likely the cause of his symptoms?

Answer: The combined use of didanosine and stavudine is no longer recommended by the DHHS guidelines due to the increased risk of pancreatitis, hepatic steatosis and lactic acidosis. Both didanosine and stavudine have other overlapping toxicities such as peripheral neuropathy, which also requires them not to be combined.

The patients ARV regimen is changed from Nelfinavir, stavudine and didanosine to nelfinavir, didanosine and tenofovir. Is this correct?

Answer: Studies have demonstrated that patients receiving didanosine and tenofovir together have a less robust increase in CD4 counts. This patient should avoid this combination if possible. Since the nelfinavir, stavudine, and didanosine was his first regimen, he will likely respond to preferred NRTI backbones, such as tenofovir/ emtricitabine or zidovudine/lamivudine, assuming his lab work allow for these medications to be given. Of note is the fact that he is on a non-preferred protease inhibitor as well. Since his viral load is undetectable, you may consider switching, but it would not be wrong to continue the nelfinavir assuming he is not experiencing significant diarrhea.

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TABLE 1. Antiretroviral Components Not Recommended as Initial Therapy

Antiretroviral drugs or regimens *(in alphabetical order)*	Special circumstances in which the drugs or regimens may be used
Darunavir (ritonavir-boosted) (DIII)	• Lack of data in treatment-naïve patients
Delavirdine (DII)	• Inferior virologic efficacy • Inconvenient (three times daily) dosing
Didanosine + tenofovir (DII)	• High rate of early virologic failure • Rapid selection of resistant mutations • Potential for immunologic non-response/CD4+ decline
Enfuvirtide (DIII as initial regimen)	• No clinical trial experience in treatment-naïve patients • Requires twice-daily subcutaneous injections
Indinavir (unboosted) (DIII)	• Inconvenient dosing (three times daily with meal restrictions) • Fluid Requirement
Indinavir (ritonavir-boosted) (DII)	• High incidence of nephrolithiasis
Ritonavir as sole PI (DIII)	• High pill burden • Gastrointestinal intolerance
Saquinavir (unboosted) (DII)	• High pill burden • Inferior virologic efficacy
Tipranavir (ritonavir-boosted) (DIII)	• Lack of data in treatment-naïve patients
Zalcitabine + zidovudine (DII)	• Inferior virologic efficacy • Higher rate of adverse effects than other dual-NRTI alternatives

Adapted from DHHS. 2006.

TABLE 2. Antiretroviral Regimens or Components That Should Not Be Offered at Any Time

	RATIONALE	EXCEPTION
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Monotherapy with NRTI or NNRTI (EII)	• Rapid development of resistance • Inferior antiretroviral activity when compared with combination of three or more antiretrovirals	• Pregnant women with pretreatment HIV RNA <1,000 copies/mL using ZDV monotherapy for prevention of perinatal HIV transmission, not for HIV treatment for the mother*; however, combination therapy is generally preferred.
Dual-NRTI regimens (EII)	• Rapid development of resistance • Inferior antiretroviral activity when compared with combination of three or more antiretrovirals	
Triple-NRTI regimens (EII) except for abacavir/zidovudine/lamivudine or possibly tenofovir + zidovudine/lamivudine	• High rate of early virologic non-response seen when triple NRTI combinations including ABC/TDF/3TC or TDF/ddI/3TC were used as initial regimen in treatment-naïve patients • Other 3-NRTI regimens have not been evaluated	• Abacavir/zidovudine/lamivudine (CII); and possibly tenofovir + zidovudine/lamivudine (DII)
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Amprenavir oral solution (EIII) in: pregnant women; children <4 yr old; patients with renal or hepatic failure; & patients on metronidazole or disulfiram	• Oral liquid contains large amount of the excipient propylene glycol, which may be toxic in the patients at risk	• No exception
Amprenavir + fosamprenavir (EII)	• Amprenavir is the active antiviral for both drugs, combined use have no benefit and may increase toxicities	• No exception
Amprenavir oral solution + ritonavir oral solution (EIII)	• The large amount of propylene glycol used as a vehicle in amprenavir oral solution may compete with ethanol (the vehicle in oral ritonavir solution) for the same metabolic pathway for elimination. This may lead to accumulation of either one of the vehicles.	• No exception
Atazanavir + indinavir (EIII)	• Potential additive hyperbilirubinemia	• No exception
Didanosine + stavudine (EIII)	• High incidence of toxicities – peripheral neuropathy, pancreatitis, and hyperlactatemia • Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women*	• When no other antiretroviral options are available and potential benefits outweigh the risks* (DIII)
Didanosine + zalcitabine (EIII)	• Additive peripheral neuropathy	• No exception
Efavirenz in first trimester of pregnancy or in women with significant childbearing potential* (EIII)	• Teratogenic in nonhuman primates	• When no other antiretroviral options are available and potential benefits outweigh the risks* (DIII)
Emtricitabine + lamivudine (EIII)	• Similar resistance profile • No potential benefit	• No exception
In vitro antagonism	• Lamivudine + Zalcitabine (EIII)	• No exception
Nevirapine initiation in treatment-naïve women with CD4 >250 cells/mm3 or in treatment-naïve men with CD4 >400 cells/mm3 (DI)	• Higher incidence of symptomatic (including serious and even fatal) hepatic events in these patient groups	• Only if the benefit clearly outweighs the risk
Saquinavir as single protease inhibitor (EIII)	• Poor oral bioavailability (4%) • Inferior antiretroviral activity when compared with other protease inhibitors	• No exception
Stavudine + zalcitabine (EIII)	• Additive peripheral neuropathy	• No exception
Stavudine + zalcitabine (EII)	• Antagonistic effect on HIV-1	• No exception

When constructing an antiretroviral regimen for an HIV-infected pregnant woman, please consult "Public Health Service Task Force Recommendations for the 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" in http://www.aidsinfo.nih.gov/guidelines/.

Adapted from DHHS. 2006.[2]

Clinically Significant Drug Interactions Between Antiretrovirals and Nonprescription Medications: Contraindicated Combinations

Linda M. Spooner, PharmD, BCPS

Introduction

The significance of drug interactions between antiretrovirals (ART) and non-prescription medications has become a major issue during the era of highly active antiretroviral therapy (HAART). The mechanisms of these interactions are either pharmacokinetic or pharmacodynamic in nature. Pharmacokinetic interactions result when one drug affects the absorption, distribution, metabolism, and excretion of another, while pharmacodynamic interactions occur when one drug acts in an additive, synergistic, or antagonistic way with another[1]. Outcomes of drug interactions are often clinically significant, resulting in adverse drug reactions (due to supratherapeutic serum concentrations or additive side effects) or development of viral resistance with subsequent treatment failure (due to subtherapeutic serum concentrations or antagonism).

Drug interactions between ART and nonprescription medications present a difficult challenge, as many prescribers and pharmacists may be completely unaware of their patients' use of over the counter (OTC) medications, since these can be purchased anywhere from convenience stores to supermarkets, and patients often do not disclose their methods of self-treatment to their healthcare providers.

It is critical for healthcare professionals to maintain a working knowledge of the literature and current treatment guidelines that address the identification and avoidance of contraindicated combinations. This brief review will emphasize a few nonprescription medications that are contraindicated with a variety of ART.

Acid-suppressive Therapies

The nonprescription proton pump inhibitor omeprazole (Prilosec OTC™) provides a full 24 hours of acid suppression. Atazanavir (Reyataz®) requires gastrointestinal acidity for optimal dissolution and absorption. Several studies demonstrate that concomitant use of proton pump inhibitors (PPIs) and atazanavir results in clinically significant decreases in atazanavir concentrations.[2,3,4] Therefore, use of PPIs in combination with atazanavir is not recommended, due to the high risk of treatment failure.[5] Similarly, the concomitant use of delavirdine (Rescriptor®) with PPIs and H2 antagonists (e.g.: Pepcid AC®) is not recommended due to reductions in delavirdine serum concentrations.[5] If a patient requires acid-suppressive therapy for occasional heartburn, antacids may be given two hours before or one hour after the dosing of these antiretrovirals.[5]

Complementary Therapy

Because complementary therapies are often utilized by patients without the knowledge of their practitioners, it is important to counsel patients that the use of these agents may cause significant drug interations with ART that may result in treatment failure.

St. John's Wort – St. John's Wort (SJW) is a commonly used complementary medicine for the treatment of mood disorders including depression and anxiety. It is a potent inducer of the 3A4 iso-enzyme of the cytochrome P450 system.[6] As a result, it significantly reduces the serum concentrations of all protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Therefore, concomitant use of SJW is contraindicated with these antiretrovirals, due to the risk of virologic failure with concomitant use.[5] Healthcare professionals should emphasize the need for avoiding the use of SJW in all patients taking PI- and NNRTI-based ART regimens due to this interaction.

Garlic – Garlic supplements are often used for hyper-lipidemia, hypertension, and coronary artery disease. Data regarding the impact of garlic on cytochrome P450 3A4 are inconsistent and conflicting. Some preparations of garlic act as inducers of this isoenzyme; one study indicated that saquinavir (Invirase®) serum concentrations are significantly decreased by garlic supplements[7], and their concomitant use is contraindicated.[5] Current recommendations do not contraindicate the use of garlic with other PIs or with NNRTIs at this point in time, but caution should be used until more data is available. Because complementary therapies are often utilized by patients without the knowledge of their practitioners, it is important to counsel patients that the use of these agents may cause significant drug interactions with ART that may result in treatment failure.

Conclusion

Many patients believe that nonprescription medications are safe because they are available over the counter. However, concomitant use of several commonly used OTC products may result in virologic failure when combined with certain PIs or NNRTIs. It is vital that practitioners obtain a thorough medication history from each patient, including all nonprescription medications, by asking specifically about OTC and herbal/complementary medication use. Practitioners should emphasize the importance of contacting the prescriber or pharmacist prior to using any nonprescription product. Healthcare professionals must maintain current drug information databases in order to assist with identification of these interactions.

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Increased Number of Reported Invasive *Streptococcus pneumoniae* Cases, Newark, 2006

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The majority of HIV specialists believe that the potential benefit of pneumococcal vaccination in the United States outweighs the risk.

The New Jersey Department of Health and Senior Services (NJDHSS) and the Newark Health Department have observed an increased number of invasive *Streptococcus pneumoniae* cases among adults and adolescents in the Newark area. Over a third of the reported cases occurred in HIV infected persons.

When seeing patients, it is important to review their immunization status. HIV infected adults and adolescents who have a CD4+ T lymphocyte count of >200 cells/µL should be administered a single dose of 23-valent polysaccharide pneumococcal vaccine (PPV) if they have not received this vaccine during the previous five years. The majority of HIV specialists believe that the potential benefit of pneumococcal vaccination in the United States outweighs the risk. Pneumoccocal immunization should also be considered for patients with CD4+ T lymphocyte counts of <200 cells/µL. However, clinical evidence has not confirmed its efficacy. There-fore, revaccination can be considered for patients who were initially immunized when their CD4+ T lymphocyte counts were <200 cells/µL and whose CD4+ counts have increased to >200 cells/µL in response to Highly Active Antiretroviral Therapy (HAART). The recommendation to vaccinate is increasingly important due to the increasing incidence of invasive infections with drug-resistant (including TMP-SMZ-, macrolide-, and ß-lactam--resistant) strains of *Streptoococcus pneumoniae*.[1] Immunization with pneumococcal polysaccharide vaccine is 60-70% effective in preventing invasive disease. The vaccine may be less effective in preventing pneumococcal infection in some groups, particularly those with significant underlying illness. Although, the vaccine may be as effective in some persons, especially those who do not have normal resistance to infection, it is still recommended for such persons because they are at high risk of developing severe disease.[2]

The duration of the protective effect of primary pneumococcal vaccination is unknown. Periodic revaccination can be considered; an interval of 5 years has been recommended for persons not infected with HIV and also might be appropriate for persons infected with HIV. However, no evidence confirms the clinical benefit from revaccination.[1] A list of upcoming influenza and pneumococcal immunization events can be found at www.nj.gov/health/flu/schedules.shtml. For questions regarding immunization events, please contact the agency sponsoring the event.

The New Jersey Administrative Code (N.J.A.C. 8:57-1.8) stipulates that laboratories and health care providers report all cases of *Streptococcus pneumoniae* from a normally sterile site, (e.g. blood, cerebrospinal fluid), to the local health officer having jurisdiction over the locality in which the patient lives, or, if unknown, to the health officer in whose jurisdiction the health care provider requesting the laboratory examination is located.

For additional information on reporting cases of *Streptococcus pneumoniae*, please contact your local health department or the New Jersey Department of Health and Senior Services at 609-588-7500.

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Association of Nurses in AIDS Care (ANAC) 2006 Conference Report

Debbie Mohammed, MS, MPH, BSN, APRN-BC, ACRN

The Association of Nurses in AIDS Care (ANAC) met on October 26-29, 2006, in Las Vegas, Nevada, for their 19th Annual conference, with a theme of "Scaling the Heights of HIV/AIDS Nursing."

The opening keynote was presented by Padraig O'Malley, a public policy analyst who has documented the transition of South Africa from apartheid to democracy. He has been resident in South Africa and is now documenting the effects of the HIV epidemic.

He observed that the impact of HIV/AIDS in South Africa is best viewed through the lens of apartheid, as the current leaders have assumed an attitude of denial and are committing an act of 'Silent Genocide' on their countrymen. There is a double system of healthcare: a private system where life-saving antiretrovirals are available and a public system where there is a lack of human resources (nurses) and life saving medications. Without the strong voice of Nelson Mandela agitating for access to healthcare and medications, the international community has provided unspoken acquiescence to the atrocities imposed on the poverty stricken populace.

O'Malley starkly observed that people spend most of their time outside of work attending funerals and that coffin making is the main industry in the township closest to where he lives, making the reality of death faced by the South Africans up close and real.

The inadequate availability of nurses in this country has been exacerbated by the closure of nursing schools to balance the national budget and put it in a favorable light with the International Monetary Fund and the World Bank. Working conditions with higher pay are better in private medical care facilities, and the lure of nurse recruiters from the United States and England depletes an already scarce human resource.

Nurses in South Africa may not be in a better position than their poverty stricken patients. They work for about $400 US/month. One in every 6 RNS is infected with HIV disease and has to deal with the stigma of having the disease, as well as the stigma of taking care of patients who are HIV infected. In the hospital wards at least one patient dies every day, and nurses function as the 'Chief Cook and Bottle Washer.' Management styles at the hospital are hierarchal, and poor record keeping is the norm.

(Continued on next page)

Association of Nurses in AIDS Care (ANAC) 2006 Conference Report

(Continued from previous page)

The silver lining to this cloud is the resilience, initiative and commitment of South African women generally and Nurses specifically. O'Malley thinks that this may be the life saving grace of South Africa, together with an outcry from the international community for real change within this country.

It was a surprise when Warren Hewitt, a doctoral student in public health policy at Morgan State University, Baltimore, Maryland, reiterated similar views about the United States, seen through the lens of slavery. He noted that the United States spends more on healthcare than any other country; however, about 15-20% of Americans are unable to access healthcare. He contends that residential segregation has contributed the most to this unequal access to care. Other causes of health disparity in African Americans include: the rates of chronic diseases, the adverse effects of slavery which are still apparent in America, African Americans may have been relegated to second class citizenship, and there may be institutional barriers to services with differential therapies based on race and a compromised commitment to wellness.

Deborah Parham Hopson, Associate Administrator of the HIV/AIDS Bureau at the Health Resources and Services Administration in the Department of Health and Human Services, presented key areas in which nurses could be involved and make a difference. Her first point addressed the recurring theme of health disparities in the United States and in the care of African Americans and HIV/AIDS specifically. She urged the audience to tackle this problem in a culturally competent manner.

HIV prevention is an effective tool in halting the epidemic in the United States. She underlined the importance of primary prevention measures in populations most at risk: teenagers, minorities and MSM. She noted that Prevention with Positives is an especially effective tool in slowing down the epidemic, as HIV-positive people who are aware of their HIV status and care about their partners will make an attempt to keep their partners safe.

The issue which drew the most discussion by attendees and garnered the most trepidation was the upcoming Reauthorization of the Ryan White Care Act, which has been delayed in the Senate. Parham Hopson noted that until the Act is authorized, current programs will continue to be funded as partial grants. If the Act is not reauthorized then systems of care will be severely impacted and patient's healthcare status will be severely compromised.

At the local level it is imperative that safety nets stay intact for patients who utilize Ryan White funding as the payer of last resort. Medicare Part D has imposed specific challenges in the availability of medications. Health care providers have to make this payment source work for patients.

It is imperative that the national deficit be reduced as small increases in federal spending impacts the availability of resources directed towards healthcare and to HIV care specifically.

The prevalence of HIV disease is increasing in the over-fifty population. Other chronic diseases are causing deaths, and increasing morbidity among this population. One should be responsive to these co-morbid diseases in HIV positive individuals and treat in a comprehensive manner.

Dr. Parham Hopson urged that one pay attention not only to the national picture of the epidemic but also to consider the impact of the disease internationally in Sub Saharan Africa, Asia, Europe, Latin America and the Caribbean. She praised the international work of ANAC members including Mary Anne Vitiello and Jennifer Okonsky of New Jersey.

In our clinics, we should continue to support and educate patients to be adherent to their medications and how to cope with side effects of their medications now that we are able to minimize their pill burden.

Communication among healthcare providers is especially important to prevent burnout and prevention fatigue.

Lastly, the new CDC guidelines for implementing Routine HIV Testing are not law and we must carefully think about how to implement them within our medical care sites.

Despite coming from three different backgrounds, it was amazing how similar the messages were from different keynote speakers, on different days at this conference. Health disparities among non-white persons with HIV disease were underscored, and the role of nurses in empowering patients towards optimum health status was acknowledged. The expectation for nurses in AIDS care is that we will continue to champion the rights of our patients for high quality care.

■ **To find out more about membership and the activities of the New Jersey Chapter of the Association of Nurses in AIDSCare, contact Debbie at: debbiemoha@aol.com or (973) 972-9827.**

Debbie Mohammed, MS, MPH, BSN, APRN-BC, ACRN, is President of ANAC NJ for 2007. She is an Advanced Practice Nurse in the Infectious Diseases Clinic, and is Project Director for Rapid HIV Testing at UMDNJ-University Hospital in Newark

New Jersey Department of Health and Senior Services Rapid HIV Testing Team Receives ASTHO Vision Award

(Continued from page 1)

The NJDHSS partnered with private hospitals, community health centers, and service organizations to expand the rapid HIV testing program. The Robert Wood Johnson Medical School manages and serves as the laboratory director for the majority of the laboratories performing the tests, significantly reducing the cost to local clinics, and standardizing equipment and performance across the state.

For more information on rapid HIV testing in New Jersey, visit:
www.state.nj.us/health/aids/Rapid testing or call the New Jersey HIV Helpline at 1-866-HIV-CHEC.

References

1. National Center for Health Statistics. Tracking Healthy People 2010. Centers for Disease Control and Prevention. Available at: http://www.healthypeople.gov/Document/tableofcontents.htm#tracking
2. Center for Health Statistics. Healthy New Jersey 2010 Update 2005. New Jersey Department of Health and Senior Services. Available at: http://www.state.nj.us /health/chs/hnj2010u05/index.shtml

GUIDELINES AND STATISTICS

New Jersey Department of Health & Senior Services Division of HIV/AIDS Services (DHAS)
www.state.nj.us/health/aids/aidsprv
NJ HIV/AIDS Semi-annual Newsletter (statistical report); policies, and guidelines for HIV/AIDS care and services in New Jersey
New Jersey rapid testing site: www.state.nj.us/health/aids/rapid testing

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

New Jersey AIDS/STD Hotline: (800) 624-2377
- 24-hour professionally-staffed service
- Consultation, testing referrals, free materials

US Dept. of Health & Human Services
www.aidsinfo.nih.gov • 1-800-HIV-0440 (1-800-448-0440)
HIV/AIDS treatment guidelines; prevention, treatment, and research.
National Institutes of Health-sponsored searchable clinical trials database: http://clinicaltrials.gov

CDC National Prevention Information Network (NPIN)
HIV, STD, and TB news, funding,materials, conference and satellite broadcast announcements.
http://www.cdcnpin.org

Centers for Disease Control (CDC) – Division of HIV/AIDS Prevention
HIV/AIDS research, surveillance reports, funding announcements, research and reporting software, epidemiology slide sets
http://www.cdc.gov/hiv/hivinfo.htm#WWW
Rapid Testing: http://www.cdc.gov/hiv/rapid_testing
MMWR [Morbidity and Mortality Weekly reports]:
http://www.cdc.gov/hiv/pubs/mmwr.htm

FDA MedWatch
Updated reports on medication interactions and warnings:
1-800-FDA-1088; Subscribe to e-bulletin:
http://www.fda.gov/medwatch/elist.htm

National HIV/AIDS Clinicians' Consultation Center
http://www.ucsf.edu/hivcntr
Consultation on antiretroviral therapy, drug resistance, opportunistic infection prophylaxis and treatment, laboratory evaluation; occupational exposure, perinatal intervention.
Warmline: 800-933-3413
National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline): 888-448-4911 (888-HIV-4911)
National Perinatal HIV Consultation and Referral Service: 888-448-8765 (888-HIV-8765)

HIV/AIDS TRAINING

HIV/AIDS MEDICAL UPDATE SERIES
Free On-site Training

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

To schedule a free 1-hour HIV medical education program at your health care site on any of these topics, contact Kimi Nakata at (973) 972-1246 or ccnakata@umdnj.edu

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

University of Medicine & Dentistry of NJ Center for Continuing and Outreach Education Division of AIDS Education
www.umdnj.edu/ccoe/aids
Conferences, training for HIV/AIDS health and social service professionals.

Free online CME/CE – topics include:
- HIV and Hepatitis C Virus Co-Infection
- Rapid Diagnostic Testing for HIV (updated 6/06)
- Recommendations to Reduce Occupational HIV Transmission
- Treatment of Tuberculosis in Patients Infected with HIV
- Hepatitis B and HIV Co-Infection
- Beyond HIV: Lesbian, Gay Bisexual and Transgender (LGBT) Health
- Immunization for HIV Infected Children and Adolescents
- Reducing Vertical HIV Transmission in NJ

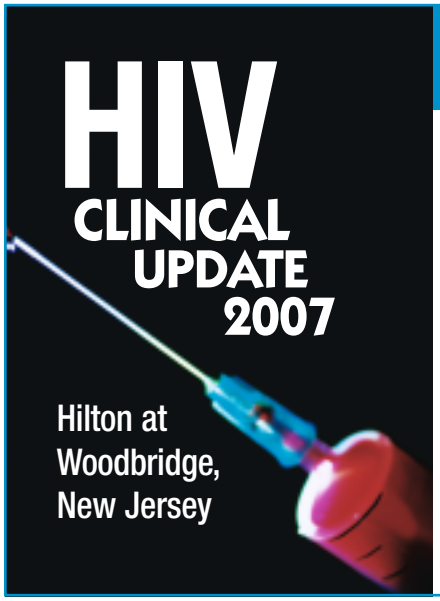
NY/NJ AIDS Education And Training Centers (AETC)
New York/New Jersey regional training calendar, resource directory, clinician support tools and references including training slide sets, wall charts. http://www.nynjaetc.org

AIDS Education and Training Centers (AETC)
National Resource Center www.aids-etc.org
HIV treatment guidelines, training materials/curricula, evaluation tools, Daily HIV/AIDS Treatment News; clinical resources including PDA tools

STD/HIV Prevention Training Centers (PTC)
Medical: www.nyc.gov/html/doh/html/std/ptc.shtml
Behavioral: www.urmc.rochester.edu/chbt

Title X Family Planning Regional Training Center (RTC)
[DHHS/OPA funded]: training www.cicatelli.org/titlex/home

Northeast Addiction Technology Transfer Center (NEATTC)
Addiction training, treatment news: http://www.neattc.org



SAVE THE DATE: THURSDAY, JUNE 14, 2007

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

Full conference information:
www.umdnj.edu.ccoe/aids
Course Code: 07HH04

Michelle Thompson:
(973) 972-1293 or ccthomps@umdnj.edu

David Rosen: (973) 972-6325 or rosendv@umdnj.edu

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