



Hepp News

HIV Education Prison Project

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About

HEPP News, a forum for correctional problem solving, evolved out of ongoing discussions among HIV specialists based at the Brown University AIDS Program about the need for HIV updates designed for practitioners in the correctional setting. The board of editors includes national and regional correctional professionals, selected on the basis of their experience with HIV care in the correctional environment and their familiarity with current HIV treatment. HEPP News targets correctional administrators and HIV/AIDS care providers including physicians, nurses, outreach workers and case managers. Published monthly and distributed by fax, HEPP News provides up-to-the-moment information on HIV treatment, efficient approaches to administering such treatments in the correctional environment, national and international news related to HIV in prisons and jails, and correctional trends that impact HIV treatment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education to physicians who accurately respond to the questions on the last page of the newsletter; please see last page for details.

The editorial board and contributors to HEPP News are well aware of the critical role prisons and jails play in the treatment and prevention of HIV. The goal of HEPP News is to provide reports of effective and cost-conscious HIV care that can truly be implemented within the correctional environment. We hope this newsletter achieves that goal.

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Update On Antiretroviral Therapy

David Paar, M.D.
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Texas Department of Corrections
Speaker's Bureau: Roche Pharmaceuticals;
Educational Grant: Glaxo Wellcome, Merck
Immune Response Corp., Pfizer

In 1996, the Department of Health and Human Services (DHHS) and the Henry J. Kaiser Family Foundation invited a group of experienced clinicians and researchers to form the Panel on Clinical Practices for Treatment of HIV Infection. Following a comprehensive review of the scientific literature and current clinical practice regarding antiretroviral therapy for HIV infection, the panel formulated Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents. (Carpenter CC et al.; Antiretroviral therapy for HIV infection in 1996. Recommendations of an international panel. International AIDS Society-USA. JAMA. 276(2):146-54: 1996) The guidelines are updated periodically. This article reviews the December 1, 1998 update and includes other pertinent information not specified in the guidelines. The complete guidelines can be obtained from the HIV/AIDS Treatment Information Service (ATIS) (phone: 1-800-448-0440, fax 301-519-6616) or the ATIS website (<http://www.hivatis.org>). See also box on page 6 entitled *Initial Antiretroviral Therapy*.

Viral Load

Viral load testing remains the most important clinical tool in determining prognosis and response to antiretroviral therapy in people with HIV infection. The new guidelines indicate that 2 - 8 weeks (as opposed to 4 - 8 weeks) should be sufficient to see a significant reduction in viral load indicative of effective therapy. Recent data suggest that a lack of a reduction in HIV-1 RNA to <1,000 copies/mL after four weeks of HAART is strongly correlated with virologic failure.

The use of ultrasensitive viral load assays that quantitate to 20 - 50 copies/mL of HIV-1 RNA are discussed since preliminary data from ongoing clinical trials indicates that reductions of plasma viral RNA to less than 50 copies/mL are associated with a more durable response to treatment when compared to reductions of 50 - 500 copies/mL. Nonetheless, there is no clear recommendation that the more sensitive assays be used or that the definition of treatment failure be changed from 500 HIV RNA copies/mL.

Many clinicians now use the ultrasensitive assays when standard viral load assays become undetectable and the patient is willing to consider intensification of therapy if the ultrasensitive result is not less than 50 copies/mL.

Intensification means addition of another agent to a regimen that appears effective using the 500 copies/mL criteria in order to reduce the viral load to less than 50 copies/mL by the ultrasensitive assay. One must balance the potential for additional toxicities, drug interactions, and increased cost of antiretrovirals with the potential increased cost of HIV progression, and cost of more complex antiretroviral regimens should the first therapy fail. The correctional setting may pose special

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Letter From The Editor . . .

Happy New Year! The beginning of 1999 offers more promises, choices, and challenges in the use of antiretroviral therapy. In this issue, Dr. Paar has outlined the new guidelines, updated from the U.S. Public Health Service. Such guidelines are intended to reflect the minimal standard to care, and may not currently reflect Best Practice Guidelines, that many HIV specialists currently use to treat patients with HIV infection. For instance, current guidelines do not recommend using the ultrasensitive viral load assay, nor do they recommend intensification or change in therapy if HIV-1 RNA levels are not less than 1,000 copies/mL after four weeks of therapy or if not less than 50 copies after six months of therapy. Recent data demonstrate viral "rebound", or virologic failure, more rapidly among patients whose viral load is not suppressed below 50 copies, compared to those whose maximal viral suppression was between 50-400 copies/mL. Thus, Best Practices might include using the standard viral load assay before initiating therapy, and the ultrasensitive assay to monitor the antiviral response. Additionally, prisoners do not have access to clinic trials to be considered for change or intensification of therapy protocols if they do not achieve a maximally suppressed viral load. Therefore, we must make decisions, in conjunction with our patients, regarding the risks of change or intensification of therapy if complete suppression of HIV is not achieved. The continual progress made in HIV therapeutics and lack of access to clinical trials in prisons have challenged HIV specialists to push the envelope of therapy, and implement Best Practice Guidelines based on our understanding of HIV pathogenesis and therapeutics.

Dr. Flanigan summarizes the important issues of implementing cost-effective opportunistic infection prophylaxis among HIV infected patients. It remains true that an ounce of prevention is worth a pound of cure, particularly in correctional settings where there is fierce competition for health care dollars. OI prophylaxis remains one of the cornerstones of HIV care despite the recent excitement about HIV therapeutics. Indeed, one of the best prevention interventions is the optimal management of HIV replication, leading to increased CD4 counts, and after time, improvement of immune function. Of course, the immune reconstitution that occurs after starting HAART may be associated with the presentation of an occult opportunistic infection (e.g., MAC) that does not become clinically apparent until the CD4 count increases. The controversy about what to do in the setting of immune improvement is complemented by a case presentation with thoughtful discussion by Drs. Szebenyi and Tabet. They astutely discuss the intriguing issue of immune reconstitution and the role of OI prophylaxis in this setting.

Lastly, a table is provided to discuss the relative merits of multiple different types of dispensation of HIV therapy. It is unlikely that any one model of dispensation will prevail in the real world setting of diverse correctional institutions. Models that take the opportunity to teach inmates to take complex medications and eventually lead to patient autonomy are likely to have the best long term benefit for the incarcerated patient, particularly as they transfer from the correctional system to the community.

For the treatment of HIV infection, many physicians opt to use medications that are not indicated by the FDA. FDA approval does not necessarily address the use of these medications in combination or in dosages addressed in this newsletter. The learning objectives for clinicians reading this newsletter include the ability to discuss recent updates to the USPHS/IDSA guidelines and the use of a new NNRTI, Efavirenz. Clinicians should also be able to describe current treatment of opportunistic infection and the use of ultrasensitive viral load assays in the management of HIV disease.

Rick Altice MD

Update On Antiretroviral Therapy

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challenges that may make intensification difficult to implement, and one may exercise this option based on their unique circumstances until more is known about the potential benefits and risks that might result.

New Drugs

Efavirenz (EFV, Sustiva®) is a novel NNRTI (non-nucleoside reverse transcriptase inhibitor) which, when used in combination with 2 NRTIs (nucleoside reverse transcriptase inhibitor), has resulted in sustained viral load suppression to undetectable levels for greater than 1 year. Additionally, in head to head comparison of the combinations of EFV + ZDV + 3TC and IDV + ZDV + 3TC, suppression of viral replication was similar at 36 weeks. EFV, the first approved antiretroviral for daily use, is supplied as 200 mg tablets, and the dosage is 600 mg once per day. The primary side effects are rash; CNS side effects such as dizziness or vertigo and unpleasant dreams that may last 2-4 weeks; and elevation of hepatic transaminases. Rashes are usually mild and do not require

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Opportunistic Infection Prophylaxis In The Era Of Highly Active Antiretroviral Therapy (HAART)

Article by Timothy P. Flanigan, MD; BMS, Speaker's Bureau; Glaxo Wellcome, Speaker's Bureau; Merck Speaker's Bureau; Dupont, Speaker's Bureau. Adapted from: Centers for Disease Control and Prevention. "1997 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with HIV. MMWR 1997; 46 (RR-12), and Prevention and Treatment of Tuberculosis Among Patients Infected with HIV: Principles of Therapy and Revised Recommendations. MMWR; 47 (RR-20). Free copies of MMWR reports can be obtained by calling CDC National Prevention Network (800.458.5231) or by visiting the CDC website (<http://www.cdc.gov/epo/mmw>).

Now that we are in the throes of an HIV treatment revolution, where we can measure viral load and juggle complex antiviral regimens, there is the temptation to overlook opportunistic infection (OI) prophylaxis. Many of the early advances in morbidity and mortality in the care of HIV-infected patients were in the area of OI prophylaxis. For example, the widespread use of trimethoprim/sulfamethoxazole (TMP-SMZ) for prophylaxis of both *Pneumocystis pneumonia* (PCP) and toxoplasmosis was both cost-effective and led to improved quality of life and longevity in individuals with CD4 counts below 200 cells/mL.

Incarceration, paradoxically, is a

unique opportunity to identify HIV-infected individuals who may not have had prior access to HIV testing or care, and to initiate OI prophylaxis. The first step in appropriate prophylaxis is obviously diagnosis of HIV infection, followed by education and counseling for the individual with immunodeficiency. Currently, PCP is most commonly diagnosed among individuals with undiagnosed HIV infection, and therefore never prescribed appropriate prophylactic medications to prevent PCP.

Additionally, for many HIV-infected prisoners who may not have utilized nor had access to primary care in the community setting, incarceration provides the opportunity to re-address the importance of OI prophylaxis in conjunction with antiretroviral therapy. Because incarceration may provide an HIV-infected individual with a period of sobriety, issues such as substance abuse, which may complicate adherence to medications, can be addressed in the context of antiretroviral therapy and OI prophylactic treatment.

OI prophylaxis provides maximal health benefit with a very favorable cost

benefit ratio.

Targeted education and counseling regarding the importance of OI prophylaxis is an essential part of comprehensive health care for HIV-infected persons who are immunosuppressed. Patients need to be taught that prophylactic medications are necessary to keep them healthy while allowing our potent combination antiretroviral therapies time to reconstitute the immune system. In the following section, The next section will discuss recommendations for OI prophylaxis of selected opportunistic infections. (See HIV 101 below for summary).

PCP

PCP remains the most common OI among individuals with CD4 counts below 200 cells/mL. Prophylaxis for PCP is enormously effective, inexpensive, and generally well tolerated. TMP-SMZ, either one double- or single- strength tablet per day, is the preferred agent. Toxoplasmosis, the most common OI of the CNS among individuals whose CD4 count is below 100 cells/mL, and bacterial infections, which increasingly occur with advanced disease, are effective.

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HIV 101

Summary of OI Prophylaxis

Opportunistic Infection	CD4 Count Threshold for Prophylaxis	Recommended Prophylactic Drug and Dosage	Alternative Drug
<i>Pneumocystis carinii</i> Pneumonia (PCP)	CD4 \leq 200	TMP-SMZ 1DS QD -or- 1SS QD	TMP-SMZ one DS 3x/wk; dapsone 100mg QD; atovaquone 750 mg BID; aerosolized pentamidine 300mg Q month
Tuberculosis (TB)	All CD4 Counts If PPD (+)	Isoniazid (INH) with pyridoxine (9-12 months**) 300 mg QD -or- 900 mg 2x/wk	Rifampin and pyrazinamide (daily for 2 months***)
<i>Mycobacterium avium</i> Complex (MAC)	CD4 \leq 50	Macrolide antibiotics such as arithromycin (1200mg 1x/wk) or clarithromycin (500 mg BID)	Rifabutin 300mg QD
Toxoplasmosis	CD4 \leq 100 If Toxo IgG Ab(+)	TMP-SMZ one DS or SS QD	Dapsone 100mg QD + pyrimethamine 50mg QWk + leucovorin 25mg QWk

Note: CMV px not routinely recommended. *12 months is preferred. **This table is derived from the MMWR referenced above

Opportunistic Infection

continued from page 3

tively prevented among those taking TMP-SMZ. Because TMP-SMZ is inexpensive, and very effective against more than one OI, it is clearly the agent of choice for PCP prophylaxis and efforts should be made to initiate and maintain patients on this therapy. On the other hand, approximately 25-44% of individuals may have a hypersensitivity reaction and develop an erythematous drug eruption. Such reactions necessitate discontinuation of therapy in 5% of patients; otherwise

Prophylaxis for CMV currently is only partially effective, very expensive, and poorly tolerated.

patients may continue using symptomatic treatment or undergo desensitization. When patients report a "sulfa" allergy, they should be questioned closely to confirm the history of allergic reaction. In patients who do have a clear history of a drug reaction to sulfa drugs, up to 50% of patients can be successfully desensitized. For those patients who cannot tolerate TMP-SMZ, dapsone or dapsone plus pyrimethamine (for patients whose toxoplasmosis IgG serology is positive) is effective. Other alternatives for PCP prophylaxis include atovaquone and aerosolized pentamidine.

Tuberculosis

Pulmonary tuberculosis occurs at an increased incidence, is more rapidly progressive, and is more difficult to diagnose in patients who are HIV-infected, particularly those whose CD4 count is <200/mL. For this reason, appropriate prophylaxis of individuals who are co-infected with HIV and TB is of paramount importance, particularly in the correctional setting. In this case, "prophylaxis" is actually treatment of latent mycobacterial disease. It is currently recommended that all individuals who interface with the correctional setting who are HIV-infected undergo PPD and chest X-ray testing; though not recommended, anergy skin testing may be used in some situations to detect latent tuberculosis. All HIV seropositive individuals who are PPD positive (defined as induration \leq 5 mm) should receive 9-12 months of Isoniazid (INH) and pyridoxine (B6). Alternatively, correctional health care providers may utilize ultra-short course therapy with rifampin and pyrazinamide daily for two months; this may not be a useful strate-

gy in patients receiving protease inhibitors. When a rifamycin must be used in the treatment of TB, rifabutin should be substituted for rifampin-containing regimens and the dosage must be reduced. Individuals who are anergic but have a history of recent exposure should be considered for prophylaxis. Consultation with a TB expert is advised. PPD testing should be performed annually, and, when suspected, the threshold for testing for TB must be extremely low and aggressive measures taken for appropriate isolation. Directly observed therapy is indicated for all diagnosed TB cases in correctional settings and is also appropriate for treatment of latent TB infection and provided as a directly observed prophylactic therapy (DOPT).

Mycobacterium avium complex (MAC)

MAC, or MAI as it was previously called, can be effectively prevented and prolong life in HIV seropositive patients whose CD4 count is < 50 cells/mL using macrolide antibiotics such as azithromycin (1200 mg weekly), or clarithromycin (500 mg BID). The use of macrolide antibiotics for the prevention of MAC also decreases the incidence of other bacterial infections (pneumonia, bronchitis, and sinusitis) and PCP. When macrolides cannot be used, rifabutin will decrease the incidence of MAC, however provides no survival benefit and may cause significant drug interactions. Clearly, in a correctional setting, once weekly azithromycin would be the preferred MAC prophylaxis regimen.

Yeast and Fungal Infections

Daily, thrice-weekly, and weekly fluconazole has been demonstrated to effectively reduce the incidence of oral and esophageal candidiasis. Its use is limited by the relative ease of treatment when diagnosed, lack of severity of the infection, the development of azole-resistant strains and the overall cost. Likewise, both fluconazole and itraconazole have been demonstrated to reduce the incidence of cryptococcal disease. The low incidence of cryptococcosis and

the expense for preventing a single episode of disease limit its usefulness. While prophylactic azole use is not currently recommended, in patients with advanced disease (CD4 <50 cells/mL) and with recurrent candida mucositis, prophylaxis using fluconazole may be warranted, especially in correctional settings where access to health services may be limited.


Cytomegalovirus (CMV)

Prophylaxis for CMV currently is only partially effective, very expensive, and poorly tolerated because of the large number of pills required, and therefore is not routinely recommended. In the future, better medications for CMV may be licensed, and we may have the ability to better detect which individuals will develop CMV disease, allowing more targeted prophylaxis.

When can prophylaxis be stopped?

It is now clear that many patients on HAART have sustained increases in CD4 lymphocytes. The initial rise in CD4 count that occurs with HAART is predominantly due to an increase in memory CD4 T-lymphocytes. After six months, though, there does appear to be an increase in naïve CD4 T-lymphocytes, which are able to respond to new infections. Many clinicians feel that it is reasonable to consider discontinuing prophylaxis in some informed and reliable patients who have

Because TMP/SMZ is most effective and least expensive, it is clearly the agent of choice and efforts should be made to initiate and maintain patients on this therapy.

maximal and sustained viral suppression and whose CD4 counts have remained above the threshold where prophylaxis would be indicated for well over six months (i.e., CD4 count > 50 cells/mL for MAC and a CD4 count > 200 cells/mL for PCP). This is particularly true for patients for whom the pill burden of prophylaxis, or complications from prophylaxis, may be interfering with antiretroviral therapy. Many patients are very encouraged when persistent rises in CD4 counts and HIV viral load measurements below detectable limits lead to discontinuation of even a few prophylactic medications. As more prospective studies evolve, we will receive better guidance regarding immune reconstitution and prophylaxis of OIs in the era of HAART. 

See also: "Ask the Experts" on page 5

Ask The Experts

OI Prophylaxis Case Presentation

An incarcerated forty-four year old man was diagnosed a year ago with advanced HIV. His initial CD4 T lymphocyte (CD4+) count was 40 cells/mL, and his viral load was 150,000. HAART was initiated (DDI, D4T, and Nelfinavir) with excellent adherence to medications. Six months ago, his CD4+ count had risen to 220 cells/mL, and his viral load was <50 copies/mL. The viral load has remained undetectable, and his CD4 count has been in the range of 250 to 350 cells/mL. His medications now include HAART, TMP-SMZ, and azithromycin. Two weeks ago, he developed a generalized erythematous rash with pruritis. TMP-SMZ was discontinued, with resolution of the rash. Rechallenge resulted in the recurrence of the rash. TMP-SMZ has now been discontinued. What should be done about his prophylaxis for opportunistic infections?

what would you do?

Expert #1

Steven Szebenyi, MD, FACP

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Roche Pharmaceuticals, Speaker's Bureau;

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There is growing evidence, particularly anecdotal, that it may be safe to discontinue prophylaxis for opportunistic infections when CD4 lymphocyte counts rise in response to HAART. The circumstances under which it may be safe, or even prudent, to stop prophylaxis remain to be elucidated in clinical trials. The issues that must be considered are reviewed by Chaisson and Moore¹, and include the risk of acquiring and/or reactivating an OI; severity of the disease; the ease and efficacy of treatment, cost-effectiveness, toxicity (including drug interactions) and the potential for resistance to the prophylactic regimen. One must also consider whether or not alternative, effective drugs are available to treat the patient if prophylaxis should fail secondary to resistance.

Since the CD4 count continues to range as low as 250, I would favor starting another drug for PCP prophylaxis. I would not prophylax for any other OI at this time. The patient has been on azithromycin, but risk for MAC dissemination or toxoplasma encephalitis at this CD4 level is fairly low (and TMP-SMZ prevents toxoplasma as well). This man has had no infectious complications of his HIV infection, a factor in favor of the ability of his immune system to prevent reactivation of pneumocystis. The role of drug resistance (as opposed to drug adherence or other factors) in the failure of primary prophylaxis for PCP is not well delineated. Furthermore, there are several reasonably effective drugs available for prophylaxis and treatment of PCP. ☞

References:

¹ Chaisson RE and Moore RD, Prevention of opportunistic infections in the era of improved antiretroviral therapy. *Journal of the Acquired Immune Deficiency Syndromes and Human Retrovirology* 16 (Suppl 1): s14-s22

² Furrer Abstract 22180 and Vazquez Abstract 22186, 12th World AIDS Conference, Geneva, June 28- July 3, 1998; and Maradona Abstract I-206, 38th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, September 24-27, 1998)

Expert #2

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Bristol-Meyers Squibb, Grant Research/Support

Merck Immune Response Corp. Grant Research/Support

This case presents a common dilemma facing practitioners and patients with regard to the risk to benefit ratio of stopping OI prophylaxis. First off, I am generally reluctant to stop OI prophylaxis given the paucity of good data on the issue. Current information on stopping MAC or PCP prophylaxis after HAART is observational and anecdotal. MAC and PCP have been reported in patients on HAART with CD4 T lymphocyte counts that have rebounded above 'prophylaxis threshold' levels. Several large observational studies² suggest that stopping PCP prophylaxis is safe in individuals on HAART without previous PCP and with CD4 T cell counts that have gone above 250. When possible, I recommend referral to an AIDS Clinical Trial Unit (ACTU), where this issue is being prospectively studied in a randomized trial.

In this case I would definitely stop MAC prophylaxis and would be comfortable stopping PCP prophylaxis after considering the following four main points:

- **Immune function.** One should take into account CD4 T lymphocyte count, how long the CD4 T lymphocytes have been increased, and the CD4 T-cell nadir. Theoretically, entire lines of antigen-specific CD4 T-cells may be lost at low counts. It appears that some lines are not immediately restored until after being on HAART for a prolonged period of time, possibly one year.

- **PCP history.** PCP recurrence is more likely in patients with previous PCP, which generally leads me to avoid discontinuing PCP prophylaxis in such individuals.

- **Tolerability of prophylaxis.** If the patient is having significant side effects then it makes it much easier to discontinue prophylaxis. Stopping a poorly tolerated medication may also lead to better HAART adherence. I would consider Dapsone in this patient but, if aerosolized Pentamidine were the next available option, then I would be more likely to stop prophylaxis.

- **Patient comfort.** The patient should be well informed and feel comfortable with the decision of whether to stop OI prophylaxis. It has been my experience that certain patients are quite reluctant to stop prophylaxis, especially if they are having no side effects. ☞

Update On Antiretroviral Therapy

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discontinuation of therapy. Evening dosing may alleviate the dizziness while the patient is asleep, when peak drug levels are highest. EFV has been associated with serious congenital birth defects of the brain in monkeys, and its use in pregnant women is contraindicated. This side effect should be carefully discussed with all women of childbearing age even if they are incarcerated.

Although EFV in combination with two NRTIs has been classified as a preferred regimen, some experts prefer to await longer-term data before endorsing this combination. The primary advantages of using EFV as initial therapy are its ease of administration, avoidance of the complications of protease inhibitors, and it saves the protease inhibitors for subsequent regimens. EFV must be used in combinations likely to completely suppress viral replication, otherwise resistance will develop rapidly. Cross-resistance to the other NNRTIs is universal. Drug interactions with EFV are perhaps more complex than most other antiretroviral agents because it both induces and inhibits the Cytochrome P450 enzyme pathway. Co-administration of EFV with Saquinavir, Nevirapine, and Delavirdine are not recommended. If co-administered with Indinavir, the Indinavir dose should be increased to 1000 mg Q8H and if co-administered with Ritonavir, the Ritonavir dose may be reduced to 500 mg po BID if symptoms of ritonavir intolerance develop. In correctional settings, careful monitoring of side-effects and provision of encouragement may be necessary during the first few weeks of therapy.

Abacavir (ABC) was recently approved by the FDA and its use is not addressed in existing guidelines. It is an extremely potent nucleoside analogue and has been studied in combination with two other nucleosides, ZDV + 3TC. Short-term data from clinical trials shows similar suppression of viral load between the combinations of ABC + ZDV + 3TC and Indinavir + ZDV + 3TC at 24 weeks. The pill count is only four tablets per day when ZDV + 3TC is administered as Combivir®, and the regimen saves both protease inhibitors and NNRTIs for subsequent regimens. Nonetheless, many experts are concerned about the potency of the combination among patients with high viral loads, the durability of the response, as well as suppression of viral replication in extravascular locations (e.g., lymph nodes).

ABC is supplied as 300 mg tablets and the dosage is 300 mg BID. The potential side effects are similar to the other nucleoside analogs with one exception: a hypersensitivity reaction. This reaction occurs in 3 - 5 % of people and is characterized by progressive nausea and vomiting, fatigue, myalgias/arthralgias, fever, and in some cases, rash that progresses over several days. When this reaction is suspected, ABC should be stopped. Rechallenge can be fatal and is absolutely contraindicated. Symptoms of hypersensitivity almost always occur within four to six weeks of initiation of ABC and are recognizable because they involve multiple systems and progress relentlessly. Patients must be educated extensively regarding the hypersensitivity reaction and the risk of rechallenge. Patients must also be

thoroughly interviewed before restarting the medication if there has been any interruption in treatment.

New Dosing Regimens

Not discussed in the guidelines is the commonplace practice of prescribing antiretrovirals using doses that are not FDA-approved. This should only be considered when there are favorable pharmacokinetic data and clinical studies demonstrating similar efficacy. Twice-daily dosing of Nelfinavir (NFV, 1250mg BID) has demonstrated similar efficacy in clinical studies where the percentage with sustained viral suppression was equivalent to TID dosing. In clinical studies comparing combinations containing TID to BID dosing of indinavir (IDV), the proportion achieving non-detectable was 90% and 64% respectively. Therefore, BID dosing of IDV should not be used unless combined with another protease inhibitor. While only validated after 8 weeks of clinical trials, Fortovase® dosed at 1600 mg BID has been used by some clinicians. Note that the total daily dose of Fortovase® is less when the BID dosage is used. Heartburn, encountered commonly with the BID dosing, may be alleviated by initiation of therapy with 800 mg to 1000 mg BID of Fortovase®, followed by 200 mg BID dose escalations every two to three days. Therapy with H2 blockers or antacids, however, may be nec-

Initial Antiretroviral Therapy

FOR ESTABLISHED HIV INFECTION

(adapted from 12/1/98 guidelines)

PREFERRED REGIMEN:

strong evidence of clinical benefit and/or sustained suppression of plasma viral load.

One choice each from column A and column B.

Drugs are listed in random, not priority, order.

Column A

Indinavir
Nelfinavir
Ritonavir
Saquinavir (soft gel caps)
Ritonavir + Saquinavir
Efavirenz

Column B

ZDV + ddI
d4T + ddI
ZDV + ddC
ZDV + 3TC
d4T + 3TC

ALTERNATIVE REGIMEN:

less likely to provide sustained viral suppression or data inadequate.

1 NNRTI (Nevirapine or Delavirdine)
+ 2 NRTIs (Column B above)

NOT GENERALLY RECOMMENDED:

Strong evidence of clinical benefit, but initial viral suppression is not sustained in most patients

2 NRTIs (Column B above)

Saquinavir (HGC) + 2 NRTIs (Column B above)

NOT RECOMMENDED:

Evidence against use, virologically undesirable, or overlapping toxicities

All monotherapies

d4T + ZDV

ddC + ddI

ddC + d4T

ddC + 3TC

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HEPPigram ... Correctional Options for Distributing HIV Medications

HEPPigram: A new feature of HEPP News providing concise solutions to correctional HIV Problems

Delivery Method	Staffing Considerations	Ability to Salvage Medications	Ability To Monitor Adherence	Patient preference**/convenience	Additional Comments
Directly Observed Therapy (DOT) – Medline Distribution Keep on Person (KOP) – monthly “bottles” or “bags”	↑ Nursing time ↑ C.O. time ↓ staff intensive	++++ -	++++ +	++ ++	Adherence depends on confidentiality of medline and medline hours. Confidentiality may be breached in housing unit, potential for waste and trafficking of meds
Keep on Person (KOP) -- weekly or daily blister packs	↑ pharmacy time ↑ Nursing time but less than with DOT	+++	++	+++	Confidentiality may be breached in housing unit, potential for waste and trafficking of meds
DOT for selected medications (e.g., protease inhibitors)	↑ Nursing time ↑ C.O. time	++	++	++	Confidentiality may be problematic at medline and may promote resistance if adherence not equal for all medications

There is no "perfect" system to administer HIV medications. Providers must balance medication expense factors with those of adherence and patient confidentiality. Administration systems where potential for waste of medication is low (DOT or modified DOT) are labor intensive but allow inmates to interface with medical staff. Medication adherence is dependent upon a number of factors. In respect to a drug distribution system they include, among others, maintaining patient confidentiality, medline availability and ability of staff to transfer medications within the institution when the patient's housing unit is changed. Patient confidentiality issues are present for all systems but may be somewhat less with KOP. Studies are needed to determine which administration system ultimately is the most cost effective and beneficial in terms of clinical outcome for our patients.

**A distribution system for HIV meds that closely mimics that of the general population is more likely to maintain patient confidentiality than one that does not. For example, where KOP is offered, opt for a combo system where DOT is used for a reasonable time frame to monitor initial adherence patterns. This can be followed by KOP, subject to patient and doctor agreements about continued adherence.

Save the Date



Bureau of Justice Assistance (BJA) National Partnership Meeting

April 6-8, 1999
Washington D.C.
(800) 468-3571.
For more information, contact:
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<http://www.sso.org/ncja>

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1999 Community Planning Leadership Summit for HIV Prevention

March 24-27, 1999
Pittsburgh Hilton & Towers, Pittsburgh, PA
Sponsored by AED, CDC, NASTAD, NMAC
For more information contact:
Harry Williams at NMAC
Tel. 202.483.6622 • Fax. 202.483.1127

American Correctional Health Services Association 1999 Training Conference

March 11-14, 1999
Sheraton Gateway
Atlanta, GA
Registration available from:
ACHSA
PO Box 10
Glenn Dale, MD 20769
or by visiting the ACHSA website at
www.corrections.com/achsa

Live Satellite Broadcast

“Adherence to HIV Therapies: HIV Treatment and Prevention Issues”

Sponsored by the HHS Joint Satellite Broadcast Workgroup
Feb. 24, 1999
1:00 - 3:00 P.M. (EST)

6th Conference on Retroviruses and Opportunistic Infections

Sponsored by the Foundation for Retrovirology and Human Health in scientific collaboration with NIAID and CDC
Jan. 31 - Feb. 4, 1999
Chicago, IL
For information contact the
Retrovirus Conference Secretariat:
Westover Management Group, Inc.
211 N. Union Street, Suite 100
Alexandria, VA 22314
Tel. 703.684.4841
email: info@retroconference.org

News Flashes

New York City . .

was the gathering place for a major conference on HIV in corrections on October 23 and 24, 1998. HEPP News editors Anne De Groot, M.D. (Brown University) and Rick Altice, M.D. (Yale University) co-organized two symposia under the umbrella title, "Current Strategies for the Treatment and Prevention of HIV in Corrections".



Presentations at the first Symposium, "Special Focus on HIV among Incarcerated Women", included a review of the principals of HIV treatment by HIV expert Charles CJ Carpenter (lead author on the HIV treatment guidelines, published annually in the Journal of the American Medical Association). The symposium also featured an excellent state-by-state review of HIV programs for incarcerated women by Arthur Brewer, M.D., reporting on the CMS program at MCI Framingham, Massachusetts; Jennifer Clark, M.D., reporting on the care of HIV infected women at the Adult Correctional Institution in Rhode Island; Ed Pesanti, M.D., describing the UConn program at the York Institution for Women in CT; Joe Morales, Deputy Superintendent, describing HIV treatment at Bedford Hills Correctional Institution in New York State; Diana Williamson, M.D., reporting on treatment of HIV infected women at Rikers Island; Sarah Steiger, RN on her role in the co-ordination of HIV care for women incarcerated in the New Jersey DOC, and Dr. Lester Lewis, reporting for the women's HIV programs in the Pennsylvania DOC. All of the speakers reported access to all FDA approved HIV medications in their facilities. Most of the programs described providing HIV care to incarcerated women using a mixed nurse-led case management / HIV specialty clinic approach. All of the programs reported problems with discontinuity of medications, and raised concerns about the development of HIV resistance when medications were discontinued.

Later on in same symposium, Roberta Richman, the warden of the Adult Correctional Institution's (RI) Women's Unit, described the process of institutionalization and how it affects incarcerated women. Kate Decou, the Deputy Superintendent of the Hampden County Correctional Center, also presented her views on the rehabilitation of incarcerated women, based on her experiences in Massachusetts. Ellen Barry, of Aid to Incarcerated Mothers, flew in from California to speak on the impact of incarceration on mother-child relationships. The final panel on the treatment of obstetric, gynecological, and sexually transmitted disease conditions among incarcerated women, featured excellent presentations by Susan Cu Uvin, M.D. (on vertical and horizontal transmission), Pam Dole, R.N., N. P., (on examining women with histories of sexual trauma), and a discussion on the role of colposcopy in screening for cervical cancer among HIV-infected incarcerated women led by Dr. Uvin and Dr. A.K. Goodman (Massachusetts General Hospital, Boston MA).

The second symposium, titled "Creating a Consensus: Adapting HIV Treatment Guidelines to Corrections," focused on adapting current HHS guidelines to the correctional setting. Dr.

Patricia Kloser of UMDNJ reviewed the guidelines, with commentary contributed by Dr. Joe Bick, Chief Medical Officer for the California DOC's HIV treatment unit in Vacaville. Later on in the day, the topic of clinical research in the correctional setting was addressed by experts in the field, including Dr. David Thomas, (Medical Director, FL DOC), Dr. David Wohl (University of North Carolina), Dr. David Paar, (UTMB at Galveston and Texas DOC), Dr. Ken Mayer, (Director of the AIDS Program Brown University, and HIVNET investigator) and Dr. Jerry Friedland (Director of the Yale University AIDS Program and CRI investigator). The symposium also featured panel presentations on harm reduction, peer education, discharge planning, treatment of hepatitis B and C, and cost-effectiveness of HIV treatment. The closing session provided information on federal programs targeting HIV in correctional settings.

Speakers included Dr. Ted Hammett, noted HIV epidemiologist, Mr. Norm Fikes of the Center for Disease Control and Prevention, Mr. Todd Summers of the White House Office of National AIDS Policy, Dr. Abe Macher of HRSA, and Dr. Judy Auerbach of the Office on AIDS Research, National Institutes of Health. These speakers unanimously reported an increasing focus by federal organizations on the diagnosis, management, and prevention of HIV infection among incarcerated individuals.

Long Beach, CA . . .

The National Commission on Correctional Health Care 22nd National Conference that took place in Long Beach, California on November 2-4 1998 also featured several presentations on the topic of HIV in corrections.



Newsletter editors Rick Altice, M.D and Anne De Groot, M.D. presented on the topics of adherence and the treatment of HIV infected, incarcerated women, respectively. Dr. Joe Bick of the California DOC presented his approach to Post-Exposure Prophylaxis (PEP), a topic he will also summarize for HEPP News, next month. Dr. Tom Conklin and Dr. Tom Lincoln presented information on their fascinating study of risk behaviors (including HIV risks) gathered at intake at the Hampden County Correctional Facility, in Massachusetts. The topic of collaborations between Public Health and Corrections was presented by Dr. Ted Hammett of Abt Associates in Cambridge, in conjunction with the National Center for HIV, STD, and TB Prevention at the CDC.

In summary, the topic of HIV treatment is becoming an omnipresent feature of correctional meetings. How will the topic of corrections fare at national meetings on HIV? Look to HEPP News next month for a review of the Keystone conference on HIV Immunopathogenesis and Vaccines, and the 6th Conference on Retroviruses and Opportunistic Infections in Chicago, 1999. ☞

WE WELCOME COMMENTS OR SUGGESTIONS.

Please direct them to the HEPP News editors at Brown University AIDS Program (BRUNAP), Brown University, Box G-H105 Providence, RI 02912
phone (401) 863-2180



Update On Antiretroviral Therapy

continued from page 6

essary to treat this side effect.

Delavirdine (Rescriptor®) and Nevirapine (Viramune®) are now specified by name, as opposed to being referred to simply as NNRTIs. This change was necessary as a result of the clinical development and inclusion of Efavirenz as a preferred regimen. Although not specified in the updated guidelines, many experts are now prescribing nevirapine as a single daily dose of 400 mg following the two week lead in period of 200 mg QD. Recent pharmacokinetic data support delavirdine dosed as 600 mg BID, however, this has not been validated in clinical trials.

Clinical data is accumulating regarding side effects and efficacy of many of the recommended combinations for people in whom prior therapy has failed. Generally, in the correctional setting, the use of less-frequent dosing of antiretrovirals improves adherence, and decreases the need for custody, nursing, and pharmacy staff to dispense medications. Updated information on these combinations can be expected in mid to late 1999.

New Notation About Adverse Events

Lactic acidosis with hepatic steatosis has been added as a rare, but potentially life threatening side effect of all of the nucleoside analogues. Fat redistribution and lipid abnormalities as well as possible increased bleeding episodes in patients with hemophilia have been added as potential side

effects to all of the protease inhibitors. In regard to lipid abnormalities, interventions may need to be undertaken when there are multiple risk factors for pancreatitis or cardiovascular disease. These interventions include discontinuation of the protease inhibitor, dietary modification, and lipid lowering agents.

Summary

In summary, correctional health care providers who treat HIV should be aware that more sensitive viral load assays, which quantitate HIV RNA to 20-50 copies/mL, are commercially available. Reduction of viral replication to less than 50 copies/mL predicts a more durable response to therapy, however; the use of ultra-sensitive assays has not been incorporated into existing guidelines. The new NNRTI Efavirenz, in combination with 2 nucleosides, is now listed as one of the preferred therapies although the durability of its efficacy beyond one year has not been proven equivalent to combination therapy with protease inhibitors. The list of adverse events for nucleosides and protease inhibitors has "officially" been expanded to include nucleoside-associated lactic acidosis with hepatic dysfunction and protease inhibitor-associated abnormalities in lipid metabolism that most HIV practitioners have been aware of for quite some time. Existing guidelines do not, however, assist in the management of more complicated patients who are heavily antiretroviral-experienced. Such challenges require the expertise of seasoned HIV specialists to interpret "beyond the guidelines." ☞

HIV Internet Resources

AIDS Treatment Data Network

<http://204.179.124.69/network>

AEGIS

<http://www.aegis.com>

ACTUP

<http://www.actupny.org>

The Body: An AIDS Information Resource

<http://www.thebody.com>

CDC NCHSTP-Divisions of HIV/AIDS Prevention

<http://www.cdc.gov/nchstp/hiv-aids/dhap.htm>

Gay Men's Health Crisis

<http://www.gmhc.org>

HIV/AIDS Treatment Information Service

<http://www.hivatis.org>

HIV Insite form UCSF

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

Immunet and AIDS Treatment News

<http://www.aids.org>

JAMA HIV/AIDS Information Center

<http://www.ama-assn.org/special/hiv/hivhome.htm>

National Library of Medicine

<http://www.nlm.nih.gov>

University of North Carolina AIDS Clinical Trials Unit

<http://www.med.unc.edu/wrkunits/2depts/medicine/hivaidsc>

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Brown University School of Medicine designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through March 15, 1999. The estimated time for completion of this activity is one hour and there is no fee for participation in this activity.

1. The USPHS/IDSA guidelines describe the:
 - a. Best Clinical Practice Guidelines
 - b. The minimum standard of care based on clinical research
 - c. both
 - d. neither

2. Which of the following viral load level is least likely to result in virological failure after six months of HAART?
 - a. HIV-1 RNA level < 1000 copies
 - b. HIV-1 RNA level < 400 copies
 - c. HIV-1 RNA level < 50 copies

3. Which of the following are NOT true regarding PCP prophylaxis?
 - a. The preferred regimen is one double-strength tablet three times per week
 - b. The preferred regimen is one double-strength table daily
 - c. Prophylaxis for PCP should be initiated when the CD4 < 200, unexplained fevers or if there is the presence of thrush.
 - d. TMP-SMZ is effective prophylaxis against PCP, bacterial infections and toxoplasmosis.
 - e. Dapsone may be used as an alternative prophylaxis agent if the patient is intolerant to TMP-SMZ.

4. Which of the following is true regarding efavirenz (Sustiva)?
 - a. it is the only antiretroviral liscensed for once daily dosing
 - b. it is preferable to dose in the evening to avoid the dizziness sometimes encountered during the first two to four weeks of therapy
 - c. most adverse side effects (dizziness, insomnia, bad dreams) abate within a few weeks of starting therapy.
 - d. it is the first NNRTI to be placed on the PRE-FERRED list of antiretroviral combinations by the USPHS/IDSA guidelines.
 - e. all of the above

5. Using Best Practice Guidelines, which of the following is true regarding the use of viral load assays?
 - a. a standard PCR assay measuring 400 to 750,000 copies/mL is best used to assess prognosis before initiating antiretroviral therapy
 - b. a recent vaccination should not affect viral load determinations
 - c. an ultrasensitive assay measure 50 to 50,000 copies/mL is best used to measure the response to anti-retroviral therapy
 - d. all of the above
 - e. none of the above

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	5 Excellent	4 Very Good	3 Fair	2 Poor	1 Very Poor
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case study	5	4	3	2	1
HIV 101	5	4	3	2	1
newsflashes	5	4	3	2	1
save the date	5	4	3	2	1
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