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# HEPP NEWS

November 2000 Vol. 3, Issue 11

HIV  
EDUCATION  
PRISON  
PROJECT

Sponsored by the Brown University School of Medicine Office of Continuing Medical Education and the Brown University AIDS Program.

## ABOUT HEPP

HEPP News, a forum for correctional problem solving, 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 HIV treatment in the correctional environment, national and international news related to HIV in prisons and jails, and changes in correctional care 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.

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In accordance with the Accreditation Council for Continuing Medical Education Standards for Commercial Support, the faculty for this activity have been asked to complete Conflict of Interest Disclosure forms. Disclosures are listed at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV unless otherwise indicated. For the treatment of HIV infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

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## THE RULES: LAW AND AIDS IN CORRECTIONS

**Mary Sylla, J.D.**, *Founder & Director, CorrectHELP*  
**David Thomas, M.D.\***, *Medical Director, Florida D.O.C.*

Strange, but true -- in America, only the incarcerated have a legal right to healthcare. This right stems from early recognition by the courts that, "the public be required to care for the prisoner, who cannot by reason of the deprivation of his liberty, care for himself." *Spicer v. Williams*, 191 N.C. 487 (1926). However, the Supreme Court did not formally recognize an inmate's constitutional right to healthcare until 1976, when the court established that "deliberate indifference to serious medical needs of prisoners" is a violation of the Eighth Amendment. This article discusses the Eighth Amendment right of incarcerated persons to medical care and examines that right in the context of inmates with HIV disease.

## THE CONSTITUTIONAL BASIS OF THE RIGHT

The right of the convicted inmate to medical care comes from the Eighth Amendment's prohibition on "cruel and unusual punishments." Although originally intended to prevent "tortures and other barbarous forms of punishment," the clause has been interpreted by the Supreme Court to include a right to medical treatment for convicted inmates that does not allow "wanton and willful infliction of pain."

Pre-trial detainees also have a right to healthcare, under the Fourteenth Amendment, which prohibits the government's denial of "life, liberty or property without due process of law." Although the pre and post-conviction rights come from separate constitutional provisions, the Supreme Court has never articulated the due process medical care standard, and the rights have been interpreted by the courts to require the same level of treatment. *Revere v. Massachusetts Gen. Hosp.*, 463 U.S. 239, 244 (1983).

## A HISTORIC CASE: ESTELLE V. GAMBLE (1976)

In *Estelle v. Gamble*, 429 U.S. 97 (1976), the Supreme Court addressed the medical needs of prisoners in the context of the Eighth Amendment.

The court held that deliberate indifference to serious medical needs is prohibited "whether the indifference is manifested by prison doctors in their response to the prisoner's needs or by prison guards in intentionally denying or delaying access to medical care or intentionally interfering with the treatment once prescribed. Regardless of how evidenced, deliberate indifference to a prisoner's serious illness or injury states a [claim under the Constitution.] *Id.* at 104-105."

*...prison officials must ensure that inmates receive adequate food, clothing, shelter and medical care.*

Note that both providers and correctional officers might, according to this interpretation of the Eighth Amendment, be held to be responsible if an HIV-infected patient failed to receive their HIV medications. However, a prisoner must provide evidence of "acts or omissions sufficiently harmful" to show deliberate indifference in order to bring an Eighth Amendment claim.

Since *Estelle*, the Supreme Court has only refined the "deliberate indifference" standard once. In 1994 the Court said that deliberate indifference ". . . [lies] somewhere between the poles of negligence at one end and purpose or knowledge at the other;" (*Farmer v. Brennan*, 511 U.S. 825, 1994). The Court affirmed an "adequacy" standard stating that ". . . prison officials must ensure that inmates receive adequate food, clothing, shelter and medical care . . ." (*id.* at 833), but went on to emphasize that "deliberate indifference" requires a culpable state of mind. Federal District Courts (the trial court in the Federal system) may interpret "ade-

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## THE RULES...

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quote" with wide discretion. On appeal to the Federal Circuit Courts—the layer of the judiciary just below the US Supreme Court—this has led to vastly varying law, especially in regards to the treatment of HIV.

### RECENT DECISIONS IN HIV CASES

#### Circuit Courts

The best way to find out how "deliberate indifference" is being interpreted in relation to HIV treatment in correctional settings is to look at recent court rulings. Only two circuit courts (the regional federal appellate courts directly below the Supreme Court) have considered treatment of HIV disease and the Eighth Amendment since the development of protease inhibitors, with drastically different results.

In *Perkins v. Kansas Dept. of Corrections*, 165 F.3d 803 (10th Cir. 1999) the patient/inmate challenged his HIV treatment which, in February 1998, consisted of AZT and 3TC, but not a protease inhibitor. The Tenth Circuit, while noting the patient's argument that "HIV will become immune to [AZT and 3TC] if he is not given a protease inhibitor," and footnoting the important role protease inhibitors play in the treatment of HIV disease, held "... prison officials have recognized his serious medical condition and are treating it. Plaintiff simply disagrees with medical staff about the treatment. This disagreement does not give rise to a claim for deliberate indifference to serious medical needs." Thus, despite good scientific data to the contrary that was available at the time, the Tenth Circuit held that denial of one component of combination therapy is simply a "disagreement" about appropriate treatment.

By contrast, the Ninth Circuit has held that denial of the full combination for two days creates a triable issue of whether the medical staff was "deliberately indifferent" to the patient/inmate's medical needs. *Sullivan v. County of Pierce*, 2000 U.S. App. LEXIS 8254 (9th Cir. 2000) In *Sullivan*, the patient/inmate did not receive his protease inhibitor because the jail pharmacy did not stock the medication, despite the fact that the medical staff testified that it was "common medical knowledge that an AIDS patient taking protease inhibitors as part of an AIDS cocktail had to remain in strict compliance with that regimen at all times and without exception lest that cocktail become ineffective." The Ninth Circuit said that, "[a]lthough jail physicians, like prison officials, enjoy wide discretion in determining what constitutes appropriate treatment, the treatment Sullivan received was far

from the medical norm. . . ." Accordingly, the court concluded that the jail was guilty of deliberate indifference.

#### District Courts

Based on the written opinions of the last several years, district court judges appear to be more willing to let HIV treatment-related claims go forward to trial, by no means guaranteeing victory, but allowing inmate/patients to have their claims heard by a jury. With two such polar opinions by the Circuit Courts, it is no wonder that District Courts are not uniform in their approach to HIV care. For instance, one Maine court held that three days in a jail without medications was sufficient cause for a jury to decide whether that was deliberate indifference (*McNally v. Prison Health Services*, 46 F.Supp.2d 49. Dist. Ct. Maine, 1999). A Virginia District Court held likewise when an inmate's medications were changed without his notification and he suffered side effects (*Taylor v. Barnett*, 105 F.Supp2d 483. E.Dist. Va. 2000). An Illinois case is particularly notable because of the inmate's persistence in requesting medications. After notifying repeatedly that she needed HIV medications, yet going without them for two weeks, the inmate was found comatose in her cell. In that case, the court held that the medical staff was not deliberately indifferent, and the claim was denied (*Rivera v. Sheehan* 1998 US District LEXIS 12880 N. Dist Ill 1998).

On the other hand, a New York Federal Court this year held that a Spanish-speaking only inmate, who missed his medications because the instructions to pick up his medications were printed in English, did not suffer deliberate indifference even though it resulted in a worsening of his condition (*Leon v. Johnson*, 96 F. Supp. 2d 244. WDNY 2000). Earlier, in 1997, in New York the court held the prison system was not deliberately indifferent when an inmate was off medications for a period of a week during transport between facilities. Again, these decisions may have turned on whether or not the providers of medication had a "culpable state of mind." As knowledge of HIV management becomes more widespread, court rulings on events such as those described in this paragraph may evolve (*Nolley v. Johnson*, 1997 U.S. Dist. LEXIS 17651. S.D.N.Y. 1997).

#### NO RESOLUTION: ALABAMA AND THE SUPREME COURT

One reason the Supreme Court takes cases is to settle differing opinions of Federal Circuit Courts of Appeals. It has not done so in this area. A district court judge in the Eleventh Circuit recently held that prison officials could not be held liable for damages for a delay in delivering HIV med-

ications of three or four days. *Edwards v. Alabama Dept. of Corrections*, 81 F. Supp. 2d 1242 (Mid. Dist Ala. 2000). That court's decision was based in large part on the controlling precedent set by the Eleventh Circuit on facts developed ten years earlier in *Harris v. Thigpen*, 941 F.2d 1495 (11th Cir. 1991). In the late 1980s, when the treatment of HIV disease was dramatically different the Eleventh Circuit held that the care for HIV in Alabama, although poor, was adequate for Alabama prisoners because of the changing nature of the treatment of the disease and poor state of health care available to the non-incarcerated in Alabama.

Thus, the district court in *Edwards*, was forced to conclude that prison officials could not be held liable for damages due to the final rulings in the *Harris* case. Under a legal defense called "qualified immunity" state actors are immune from liability for their discretionary acts unless they violate "clearly established statutory or constitutional rights of which a reasonable person would have known." Therefore, based on the Eleventh Circuit's 1987 decision in *Harris* - the Alabama DOC could reasonably believe they were, and are, operating a constitutionally adequate medical system, and are not liable for damages.

#### CONCLUSION

By no means a black and white rule, the "deliberate indifference" standard of Eighth Amendment jurisprudence gives judges wide latitude to determine the standard of medical care owed to incarcerated individuals, and, unfortunately, leaves correctional medical providers and inmate/patients without strict guidance.

Due to the fast pace at which HIV treatment changes, it is particularly difficult to determine what constitutes "deliberate indifference" in this area. Some courts are satisfied if inmates have access to some HIV care, even if out of date; others will examine a doctor's decision to change an individual inmate/patient's medical regimen. The Supreme Court is unlikely to resolve the divergence of opinions that currently exist among lower courts anytime in the near future. Since judicial process has thus far failed to provide a clear standard regarding the management of HIV disease in correctional settings, decisions regarding care remain largely in the hands of medical care providers who care for the incarcerated patient.

\*Consultant: Agouron Pharmaceuticals, Bristol-Myers Squibb  
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## LETTER FROM THE EDITOR

Dear Colleagues,

Thanksgiving is upon us, and those of us providing care to HIV-infected prisoners certainly have much to be thankful for. New treatments have led to declining death rates from opportunistic infections and cancers. Inmate initiated litigation has in some cases led to necessary changes in the provision of healthcare to the incarcerated. Slowly, there is a growing realization that the health status of prisoners affects us all, and that better linkages must be in place to provide health care to this population as it moves back and forth between jail/prison and the free world. And in California, a ballot initiative has just been passed that is intended to place a greater emphasis on treatment rather than incarceration for many of those arrested for substance abuse related crimes.

These hopeful signs are tempered by some chilling realities. An increasing prevalence of resistant HIV is leading to treatment failures. Shrinking budgets and lack of vision have hindered effective treatment partnerships. New restrictions on inmate litigation have limited the role of the courts in improving inmate health care. And worldwide, many HIV-infected prisoners still face conditions that are tantamount to a death sentence.

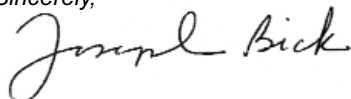
This month, Mary Sylla and David Thomas provide an overview of Law and AIDS in Corrections. Yet to be seen is whether the courts will provide a national standard for HIV care in prisons, or whether clinicians will be left to define this facility by facility.

Rick Altice provides an approach to the initiation of antiretroviral therapy in a treatment naïve inmate, and the HIV 101 provides an HIV drug update.

After reviewing this month's issue, readers should be able to identify appropriate ART regimens for treatment-naïve patients; know more about the use of the new lopinavir/ritonavir combination, Kaletra; list the responsibilities of prison officials for medical care according to US law; and understand the latest developments concerning opportunistic infections in HIV patients.

As we gather with our loved ones this year and give thanks for all of our blessings, let us not forget all that remains to be done in our struggle to improve the health care of those that society has entrusted to us.

Sincerely,



Joseph Bick, M.D.

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The editorial board and contributors to HEPP News include national and regional correctional professionals, selected on the basis of their experience with HIV care in the correctional setting and their familiarity with current HIV treatment. We encourage submissions, feed-back, and correspondence from our readership.

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## Antiretroviral Agents Dosing and Administration Recommendations

### Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

	ZIDOVUDINE (AZT, ADV, Retrovir)	DIDANOSINE (ddl, Videx)	ZALCITABINE (ddC, Hivid)	STAVUDINE (d4T, Zerit)	LAMIVUDINE (3TC, Eпивir)	ABACAVIR (ABC, Ziagen)
<b>Form</b>	100 and 300mg tabs IV vials-10mg/ml 300mg/3TC 150mg as Combivir 10mg/mL oral soln	25, 50, 100 and 150mg tabs; 100, 167 and 250 mg powder packets  200mg tabs for once daily dosing	0.375 and 0.75mg tabs	15, 20, 30, and 40mg caps 1mg/mL oral soln	150mg tabs 150mg with AZT 300mg as Combivir 10mg/mL oral soln	300mg tabs
<b>Recommended Dose</b>	300mg bid (or with 3TC as Combivir 1 tab bid)	Tablets or oral soln >60kg: 400mg qd or 200mg bid (tabs) or 250mg bid (powder)  <60kg: 250mg qd or 125mg bid (tabs) or 167mg bid (powder)	0.75mg tid	>60kg: 40mg bid <60kg: 30mg bid	150mg bid or with AZT as Combivir (1 tab bid) <50kg: 2mg/kg bid)	300mg bid
<b>Food Effect</b>	None	Levels ↓55% Take 1 hr before or 1 hr after meal	None	None	None	None Alcohol ↑ABC levels 41%
<b>Major Toxicity Class Toxicity</b>	<ul style="list-style-type: none"> <li>▪ Bone Marrow suppression: anemia and/or neutropenia</li> <li>▪ subjective complaints: GI intolerance, headache, insomnia, asthenia</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pancreatitis</li> <li>▪ Peripheral neuropathy</li> <li>▪ GI intolerance, nausea, diarrhea</li> </ul>	<ul style="list-style-type: none"> <li>▪ Peripheral neuropathy</li> <li>▪ Stomatitis</li> </ul>	Peripheral neuropathy	(minimal toxicity)	Hypersensativity (2-5%), fever, nausea, vomiting, anorexia, cough, dyspnea, malaise, morbilliform rash. May be life-threatening with rechallenge.
<b>Drug Inter-action</b>	Ribavirin may reduce AZT activity	Methadone↓ ddl levels 41%, consider ddl dose increase	Methadone↓ ddC levels 27%. No dose adjustment	None	None	None

### Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

	NEVIRAPINE (Viramune)	DELAVIRDINE (Rescriptor)	EFAVIRENZ (Sustiva)
<b>Form</b>	200mg tabs	100mg and 200mg tabs	50, 100, 200mg caps
<b>Recommended Dose</b>	200mg po qd x 14 days, then 200mg po bid	400mg po tid	600mg po qd at hs
<b>Food Effect</b>	None	None	↑50% with high fat meal; avoid after high fat meal
<b>Major Toxicity Class Toxicity</b>	<ul style="list-style-type: none"> <li>▪ Induces cytochrome P450 enzymes· PI interactions see Table 4-16 in Bartlett Guide*</li> </ul>	<ul style="list-style-type: none"> <li>▪ Methadone AUC decreased 60% titrate methadone dose</li> <li>▪ Not recommended: Ketoconazole and rifampin</li> <li>▪ Caution: anticonvulsants</li> </ul>	<ul style="list-style-type: none"> <li>▪ Inhibits and induces cytochrome P450 3A4 enzymes</li> <li>▪ Contraindicated drugs: astemizole, midazolam, triazolam, cisapride, ergot alkaloids, tergenadine</li> <li>▪ Possibly important drug interactions: rifampin, rifabutin, clarithromycin, phenobarbital, ethinyl estradiol, anticonvulsants, warfarin</li> <li>▪ PI interactions: see Table 4-16 in Bartlett Guide*</li> <li>▪ Methadone AUC decreased 60% titrate methadone dose</li> </ul>
<b>Drug Interaction</b>	<ul style="list-style-type: none"> <li>▪ Rash (15-30%) may require hospitalization; rare cases of Stevens-Johnson syndrome; hepatitis</li> </ul>	<ul style="list-style-type: none"> <li>▪ Rash; headaches</li> <li>▪ Increased transaminase levels</li> </ul>	<ul style="list-style-type: none"> <li>▪ Dizziness, "disconnectedness," somnolence, insomnia, bad dreams, confusion, amnesia, agitation, hallucinations, poor concentration</li> <li>▪ 40% usually resolves after 2 weeks</li> <li>▪ take hs.</li> <li>▪ Rash- severe in 5%; rare reports of Stevens-Johnson syndrome:</li> <li>▪ Teratogenic in cynomolgus monkeys</li> <li>▪ Avoid in pregnancy, and women and men should use adequate contraception methods.</li> <li>▪ False positive drug screening test for cannabinoids (marijuana)</li> </ul>

# ICAAC UPDATE FOR THE CORRECTIONAL PROVIDER

The 40th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) was held September 17-20, 2000 in Toronto, Canada. What follows are brief comments on data presented this year that may be clinically relevant to the care of HIV-infected inmates.

## PHARMACOKINETIC INTERACTIONS

Information was presented concerning pharmacokinetic interactions of dual protease inhibitor (PI) regimens and regimens containing both a PI and an NNRTI. Notably, efavirenz decreases the concentration of indinavir, lopinavir, and amprenavir sufficiently to raise concerns about sub therapeutic PI levels. In these situations, the use of low dose (100-200 mg p.o. bid) ritonavir can adequately raise the levels of the second PI, usually without significant side effects. In the case of Kaletra, the dose should be increased from 3 bid to 4 bid (400/100→533/133) when efavirenz is co-administered. Clearly, management of potential pharmacokinetic interactions is becoming more complex and specialized. Because incarcerated patients move from facility to facility and encounter providers with varying knowledge about doses of antiretroviral agents used in combination, opportunities for prescription errors abound. HEPP News editors believe that each system should have in place a process of routine review of medication regimens to guard against inadvertent errors.

## CASES OF DEATH IN HIV INFECTED PATIENTS

Over the past several years, it has been shown that the use of highly active antiretroviral therapy has led to decreased mortality and drop in the incidence of new opportunistic infections. A study by Jacobsen et al at Alta Bates Medical Center in California reviewed the causes of death in 56 HIV infected patients who died in 1998 and 1999. This study revealed that over half (55%) died of liver disease, cardiovascular disease, cancer, accidents, and other etiologies not directly related to HIV. Similar trends are also being seen in the correctional setting. In the California Department of Corrections' Hospice Unit in Vacaville, HIV is no longer the most common admitting diagnosis. At Vacaville, HIV related deaths fell from 72 in 1995 to 12 in 1999, in spite of an increase in patient population. This serves as a reminder that as HIV becomes more of a chronic treatable illness, we must not lose sight of the routine medical care of our HIV infected patients.

## ANTIRETROVIRAL THERAPY REGIMENS

Data was presented this year showing comparable results between NNRTI vs. PI based regimens. Additionally, there is further evidence supporting the use of single class regimens which include abacavir

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## HIV I O I ANTIRETROVIRAL AGENTS...(continued from page 4)

### Protease Inhibitors (PIs)

	INDINAVIR (Crixivan)	RITONAVIR (Norvir)	SAQUINAVIR (Invirase)	(Fortovase)	NELFINAVIR (Viracept)	AMPRENAVIR (Agenerase)
Form	200, 400, 333mg caps	100mg caps 600mg/7.5 mL po soln	200mg caps (Hard gel caps)	200mg caps (Soft gel caps)	250mg tabs 50mg/g oral powder	50, 150mg caps 15mg/mL
Recommended Dose	800mg q 8h Separated ddl dose by 1 hr	600mg bid Separate ddl dose by 2 hr	Not recommended as single PI 400mg bid with RTV	1200mg tid	1250mg bid or 750mg tid	1200mg bid
Food Effect	↑77%; take 1 hr before or 2 hours after meals; may take with low fat snack or skim milk	↑15%; take with food if possible to improve tolerability	No food effect when taken with RTV	↑6x; take with large meal unless taken with RTV	↑2-3x; take with meal or snack	high fat meal decreases AUC 20%; can be taken with or without food, but high fat meal should be avoided.
Side Effects*	GI intolerance (10-15%); nephrolithiasis or nephrotoxicity (10-15%); headache; asthenia; dizziness; rash; metallic taste; ITP; alopecia; lab: increase indirect bilirubinemia (inconsequential) Class side effects*	GI intolerance (20- 40%); paresthesias- circumoral and extremities (10%); taste perversion (10%); lab:triglyc- erides increase in 60% and transami- nase increase in 10- 15%, CPK and uric acid increase Class side effects*	GI intolerance (10-20%); increase Class effects*	GI intolerance (20-30%); headache; hypoglycemia; transaminase increase Class side effects*	Diarrhea (10-30%) Class side effects*	GI intolerance (10-30%); rash (20-25% - usually at 1-10 wks), Stevens-Johnson syndrome (1%); paresthesias (10-30% - perioral or peripheral) Increase in liver function tests. Class side effects*

\*For drug interactions with PIs, see the December issue of HEPP News. For more info on class side effects see Table 4-16 from the reference for this chart, Chapter 4 of Bartlett JG and Gallant JE. 2000-2001 Medical Management of HIV Infection. Johns Hopkins University, Baltimore, MD. 2000.

## ICAAC UPDATES... *(continued from page 5)*

as opposed to a PI or NNRTI. These non-PI options may offer enhanced tolerability and adherence, and perhaps less long term side effects. This data is tempered by some work suggesting that NNRTI and single class regimens may not fare as well in the setting of higher baseline viral loads (greater than 100,000). Additionally, a UK study of 2,111 patients who were started on therapy and followed for a median of 450 days showed that although PI and NNRTI regimens both achieved viral loads of less than 500 in similar times, NNRTI based combinations showed earlier rebound.

The new PI Kaletra (co-formulated lopinavir-ritonavir), was the big news this year, with data presented on its use in both salvage and naïve settings. Kaletra performed impressively in naïve patients, with over 80% of those treated maintaining a viral load of less than 400 at 24 weeks. Even more impressively, however, an intent to treat analysis of the use of Kaletra plus efavirenz plus 2 NRTIs in salvage therapy for those who had failed 2 PIs but were NNRTI naïve yielded at 24 weeks 82% of patients with a viral load of less than 400. The main side effects were increased cholesterol and tryglicerides. This regimen shows great promise in salvage therapy, while its role in initial therapy has potential but must be further defined.

Work was presented this year demonstrating that in the setting of virus highly resistant to AZT, hypersusceptibility to NNRTIs can develop. This may explain some of the benefit of the use of NNRTIs in the salvage setting. Other data demonstrated that virus with multiple PI resistance mutations is often less fit and therefore less able to damage the immune system. This offers a rationale for continuing treatment in those who are "failing therapy" (persistently detectable viral loads), tolerating it without side effects, and for whom no other regimens are available.

A study examined the prevalence of drug resistance in prisoners in the Texas Department of Criminal Justice as compared to patients seen at the University of Texas clinics. This work demonstrated a higher instance of some resistance patterns in prisoners and the author suggested that this may be due to factors inherent in the correctional medical delivery system. It is important to note, however, that the study did not mention whether the inmates were studied at entry to prison. The assumption appears to have been made that this resistance developed while incarcerated, when in fact patients may have presented to prison with more resistant virus. Additionally, it would be valuable to compare prisoners to a non incarcerated population which is similarly matched for co-morbid mental illness and substance abuse.

### LIPID ABNORMALITIES

Further evidence was presented concerning the increased incidence of insulin resistance in patients receiving antiretroviral therapy as demonstrated by fasting hyper-insulinemia and impaired oral glucose tolerance testing. Insulin resistance is seen in patients receiving both PI and non-PI regimens, and is associated with an increased risk for cardiovascular events. Studies attempting to correct these abnormalities by switching from a PI based regimen to an NNRTI or abacavir based regimen have met with mixed success. In patients who are NNRTI naïve, viral load reductions are usually maintained when an NNRTI is substituted for the PI. A decrease in tryglicerides and insulin resistance may be seen although total cholesterol may not change. Usually there is also no change in lipodystrophy. For those considering a change to an abacavir regimen, it should be noted that

there is an increased risk of virologic failure if there is extensive prior treatment experience with AZT.

### OPPORTUNISTIC INFECTIONS

#### Cytomegalovirus (CMV)

More data was presented that CMV disease is unlikely to progress in those whose CD-4 count has risen to >300 while on HAART. The risk does exist however for the immune reconstitution syndrome, which can include macular edema and may require steroid treatment. In those who have stopped treatment for active disease because CD4 counts rose to >300, the risk for reactivation of disease dramatically increases again if CD4 falls <50. For this reason, anti-CMV treatment should be restarted presumptively in those whose CD4 declines to <50/mm<sup>3</sup>.

#### Hepatitis C (HCV)

The United States Public Health Services (USPHS) and the Infectious Disease Society of America consider HCV to be an HIV related opportunistic infection. In the United States, approximately 30% of those who are HIV infected are also infected with HCV. Most studies have demonstrated that HIV/HCV coinfecting individuals progress more rapidly to end state liver disease than do those who are HCV infected but HIV negative. The USPHS recommends that all those who are HIV infected should be tested for HCV. All HCV infected patients should be treated. This does not mean that everyone should receive interferon, but treatment also includes patient education, including alcohol abstinence and avoidance of illicit drugs that may exacerbate liver disease. Patients should be counseled on methods to decrease transmission of HCV, and should be vaccinated for HBV and HAV if not already immune. Lastly, careful attention should be given to dose modifications of medications that are metabolized by the liver. As for treatment with interferon, there is little evidence to support this practice in those with poorly controlled HIV disease especially if the CD4 count is less than 200-300. In those with higher CD4 counts, well controlled HIV viral loads, and the absence of other contraindications, interferon with/without ribavirin may be appropriate on a case by case basis.

#### Human Papillomavirus (HPV)

Data was presented demonstrating that HIV infected individuals are more commonly infected with HPV, are on average infected with more serotypes, have a greater incidence of clinically evident disease, and are more likely to have persistent HPV infection compared to those who are not HIV infected. Additionally the risk for invasive disease is directly related to the decline in CD4 count.

### PATIENTS WITH LOW LEVEL PERSISTENT HIV VIREMIA

In spite of our best efforts, for some patients who do not maintain an undetectable viral load there is no suitable salvage regimen available. A study from Tenorio et al in Chicago compared three groups of patients: 1) those who maintained an HIV VL <50, 2) those with VLs that plateau at 50-10,000 and 3) those with VL>12,000. Notably, groups 1 and 2 had no difference in lymphoproliferative responses nor in the incidence of opportunistic infections, while group 3 performed worse in both areas. CD4 increase were as follows: group 1> group2> group 3. It was also noted that group 2, with persistent low level viremia, developed less resistance mutations than did group 3. This data is encouraging information for that group of patients who plateau at a low but detectable viral load and for whom no other suitable regimens are available.

## ASK THE EXPERT: Initiating HAART

MP is a 36-year-old African American male, newly diagnosed with HIV infection, whose CD4 lymphocyte count is 146 (10%) and HIV-1 RNA level is 122,000 copies/mL. His last HIV risk behavior was seven years ago when he injected drugs. He has been incarcerated for the past four years and reports no HIV risk behavior within prison. He has had no major illnesses and has no abnormalities on physical exam. Family history is significant for hypertension and CVA, but not for diabetes. He is immune to HBV (HBSAg negative) and is HCV antibody positive (HCV Ab positive). His CBC is normal and his hepatic transaminases are mildly elevated with an AST=66 and ALT=74. His lipids are within normal limits. The patient is extremely interested in starting antiretroviral therapy. What are the considerations for initiating antiretroviral therapy in this inmate who has two remaining years to his prison sentence?

### Response by Frederick L. Altice, M.D.\* :

In general, this is a healthy male with suppressed CD4 count and an extremely high viral load who is at high risk for progression of HIV. The first thing I would do is initiate PCP prophylaxis with TMP/SMZ. The patient's motivation makes initiation of antiretroviral therapy somewhat easier than in a patient who is not convinced of the potential benefits of treatment. One should next consider determining if this patient has any of the four characteristics associated with an increased risk for virologic failure of antiretroviral therapy (baseline resistance mutations, CD4<200, HIV-1 RNA > 100,000, and non-adherence). Since this patient appears to have seroconverted more than seven years ago, the likelihood of baseline resistance is lessened and I would therefore not order a baseline HIV genotype. Because this patient is antiretroviral naïve, I would plan ahead with appropriate adherence counseling (enforcing the message that the first shot is the best shot).

I would investigate institutional barriers to receiving ARTs, and if present, I might select agents to which mutations arise slowly (i.e. have a high barrier to genetic mutations). For some ART agents (3TC and NNRTIs) resistance can develop after a single mutation. Therefore, if medline routinely requires a 30+ minute wait, if medline staff were not skilled to ensure a complete regimen, or if a history of confiscation of medications during strip searches for those with "Keep on Person" therapy existed, I might avoid medications with a low genetic barrier to resistance in first line therapy such as 3TC and the NNRTIs (such as efavirenz, nevirapine). Lastly, since this patient has a high viral load and a reduced CD4 count, I am less enthusiastic to treat with less potent agents. I would select a regimen with maximal potency and minimal toxicity (see table 1). Irrespective of the antiretroviral combination, I would monitor LFTs carefully, given this patient's coinfection with HCV.

**TABLE 1. Examples of Initial HAART Regimens**

[D4T (stavudine) or ZDV (zidovudine)] + DDI (didanosine) + NFV (nelfinavir)  
 (D4T or ZDV) + ABC (abacavir) + NFV  
 (D4T or ZDV) + DD I + EFV (efavirenz)\*  
 (D4T or ZDV) + ABC + EFV\*

\*EFV containing regimens have been demonstrated to have similar efficacy for patients with VL greater and less than 100,000 copies. Enthusiasm for its use is tempered in some systems, which inefficient medication administration may increase risk of poor adherence. Resistance is more likely to develop in the presence of NNRTIs if adherence is poor.

Based on clinical trials of individuals with HIV-1 RNA > 100,000, I would avoid the use of nevirapine and triple nucleoside analogue therapy. Nearly any of the recommended nucleoside analogue combinations would be an acceptable initial treatment strategy. I might avoid the use of lamivudine (3TC) given this patient's increased risk for virological failure and the relative ease of developing resistance to this agent. I would also consider using any of a number of non-conventional nucleoside combinations, particularly the use of abacavir (ABC) as part of the nucleoside backbone (in combination with ZDV, DDI or D4T) given its potency. The major caveat for this approach

**TABLE 2. Dosages for Regimens with Ritonavir + Other Protease Inhibitor**

DRUG	EFFECT	RECOMMENDATIONS
Indinavir (IDV)	IDV- ↑2-5x RTV- no change	IND 400mg bid + RTV 400mg bid or IDV 800mg + RTV 100-200mg bid
Nelfinavir (NFV)	NFV- 1.5x RTV- No change	RTV 400mg bid + NFV 500-750 bid
Amprenavir (APV)	APV- ↑2.5x RTV- no change	APV 1200mg qd + RTV 200mg qd or APV 600mg bid + RTV 100mg qd. With EFV/APV/RTV use: RTV 200mg bid, APV 1200 mg bid + EFV 600mg hs.
Saquinavir (SQV)	SQV- ↑2x RTV- No change	SQV 400mg bid + RTV 400mg bid

Adapted from Bartlett JG and Gallant JE. 2000-2001 Medical Management of HIV Infection. Johns Hopkins University, Baltimore, MD. 2000.

would be if a system was not accustomed to managing the ABC Hypersensitivity Syndrome (see HEPP News, April 1999). In addition, I would consider using either efavirenz or a potent protease inhibitor. Though efavirenz would be easier to administer, there are two issues that might make efavirenz more appropriate at a later time: 1) if there were barriers to adherence, resistance would develop quickly if not taken consistently and leave the entire class of NNRTIs unavailable for future options; and 2) recent data suggesting hypersusceptibility to NNRTIs (efavirenz, nevirapine) in patients with genotypic mutations to NRTIs (AZT, 3TC, d4T, ddI, ABC) favors their use as salvage therapy.

Among the PIs, I would only consider those that are dosed twice daily. This means using nelfinavir or amprenavir alone or pharmacokinetic enhancement of saquinavir, indinavir or lopinavir with low dose ritonavir (see Table 2). Lopinavir is formulated with ritonavir as Kaletra; (see newsflashes, page 8). Ideally, among the protease inhibitors, I would consider using nelfinavir upfront since data demonstrates successful salvage therapy with other PIs in cases of nelfinavir failure. Additionally, nelfinavir's diminished effect on cytochrome P450 decreases the likelihood of drug interactions, and there is less hyperlipidemia associated with nelfinavir compared to some other PIs. The benefit of the pharmacokinetic enhancement of the PIs has not been thoroughly studied in comparison trials of other PIs, however is likely to have improved efficacy and potentially increased toxicity compared to non-enhanced use of a PI.

Lastly, because this patient has an increased risk for virologic failure, I would order a viral load every four weeks until the patient achieves a viral load (VL) of <50 copies/mL (ultrasensitive assay). If the patient failed to achieve a decrease in viral load of at least one log (90%) by four weeks, VL<400 copies by 12 weeks or < 50 copies by 24 weeks, I would consider intensification therapy using an additional agent if adherence was not the reason for virological failure. (See HEPP News, October 1999)

\*Speaker's Bureau: Agouron Pharmaceuticals, Bristol-Myers Squibb, DuPont, Glaxo Wellcome, Merck, Roche.



## SAVE THE DATES

### Request for Proposals (RFP): Equal Access Initiative- Computer Grants Program 2000/2001.

*Due Date: December 1, 2000*

100 minority community-based HIV/AIDS organizations will receive access to the Internet through a unique in-kind computer grants program.  
Contact: National Minority AIDS Council (NMAC) at 202.483.6622 or [info@nmac.org](mailto:info@nmac.org)  
Visit: [www.nmac.org/pubs/RFP2000-2001.htm](http://www.nmac.org/pubs/RFP2000-2001.htm)

### National STD Prevention Conference

*December 4-7, 2000*

*Milwaukee, WI*

Contact: Glenda Vaughn, Centers for Disease Control and Prevention  
Call: 404.639.1806  
E-mail: [ghv1@cdc.gov](mailto:ghv1@cdc.gov)

### Medical Management of AIDS: A Comprehensive Review of HIV Management - Winter Symposium

*December 7-9, 2000*

*San Francisco, CA*

Contact: Cliff Brock  
Department of Medicine UCSF  
Call: 415.476.5208  
Fax: 415.476.3542  
Email: [cme@medicine.ucsf.edu](mailto:cme@medicine.ucsf.edu)  
Visit: <http://medicine.ucsf.edu/programs/cme>

### 2001 ACA Winter Conference

*January 22-24, 2001*

*Nashville, Tennessee*

Call 1-800-222-5646, ext. 1922  
Fax: 1-301-918-1900  
Visit: [www.corrections.com/aca](http://www.corrections.com/aca)

### 8th Conference on Retroviruses and Opportunistic Infections

*February 4 -8, 2001*

*Sheraton Chicago Hotel and Towers,  
Chicago, IL*

Call: 703.535.6862  
Fax: 703.535.6899  
E-mail: [info@retroconference.org](mailto:info@retroconference.org)  
Visit: [www.retroconference.org](http://www.retroconference.org)

### Call for Abstracts: 13th National HIV/AIDS Update Conference

*March 20-23, 2001*

*San Francisco CA*

Abstract Deadline:  
December 15, 2000  
Call: 212.806.1633  
Fax: 212.806.1608  
Email: [jennifer.attonito@amfar.org](mailto:jennifer.attonito@amfar.org)  
Visit: [www.amfAR.org](http://www.amfAR.org)

## NEWS FLASHES

### High Rates of Hepatitis C in Massachusetts State Prisons

A blind test conducted last spring found that 29% of men and 39% of women in the Massachusetts' prison system have hepatitis C, while 4% of the state's inmates have tested positive for HIV. Since Massachusetts prisons are forbidden to routinely test for either HIV or hepatitis C, most inmates who do not request screening remain undiagnosed. (Conrada, Springfield Union-News, 9/25/00).

### New PI Combo: Kaletra

Sharon Walmsley of the University of Toronto reported the results of a phase II, multi-center, international double-blind study of 653 ART-naive subjects treated with either ABT-378/r (Kaletra) or nelfinavir in combination with nucleoside analogues. The results, reported at ICAAC last month, indicated that plasma HIV in the bloodstream dropped to undetectable levels in 79% of the patients taking Kaletra-based combination therapy versus participants receiving nelfinavir-based combination therapy for 40 weeks. Walmsley said she believes the easier dosing schedule and longer half-life of Kaletra, which combines lopinavir and ritonavir, were two factors in the better results, as patients were not only more compliant with Kaletra but the drug stayed longer in the body if they skipped a pill. (Walmsley S, Badley A, Beall G, et al. ICAAC 2000, Abstract #693).

### FDA Approves Enteric Coated Didanosine (Videx)

On October 31, the Food and Drug Administration approved enteric-coated didanosine (ddl; Videx). This new formulation of Videx includes delayed-release capsules that contain enteric-coated "beadlets," which allow slow release of the drug into the bloodstream over a 24-hour period. Enteric-coated didanosine may be useful for HIV-infected patients who show intolerance of the current "buffered" tablet formulation of Videx, which frequently causes diarrhea. For more information, contact: John Kouten, 609-897-2637 or

[john.kouten@bms.com](mailto:john.kouten@bms.com). (BMS Press Release, 10/31/00. Also see <http://www.fda.gov/cder/>).

### Staggering Numbers: AIDS Deaths in South African Prisons

AIDS-related deaths in South African prisons account for as much as 90% of the 1,000 natural deaths in South Africa this year. Since 1995, AIDS-related deaths in South African prisons have risen 300%. Gideon Morris, secretary of the Office of the Inspecting Judge, South Africa, attributes this increase in deaths to high incidence of rape and increasing number of inmates with HIV infection. (Agence France Presse, 10/17/00. [www.afp.com](http://www.afp.com)).

### HIV Among Prison Inmates in Russia

Approximately 700 HIV-infected patients reside in the Kaliningrad regional penal system in Russia. There are 46,000 registered AIDS cases nationwide, Russian Health Ministry statistics show; however, WHO officials say the actual number could be 10 times higher. The inmates are given a special diet to help them stay strong against HIV, but Western AZT-type drugs that boost the immune system are too costly, and the prisoners often must make do as best they can. (Ittner, Phil. San Francisco Chronicle, 10/16/00. P. A11; [www.sfgate.com](http://www.sfgate.com))

### Correction: Fax-back Survey

On Monday, November 6, HEPP News subscribers received a fax-back survey to provide us feedback on the newsletter. We incorrectly listed *Agouron* as our sole sponsor. HEPP News is extremely grateful for the support provided through *Abbott, Bristol Myers-Squibb, Dupont, Glaxo, Merck, Roche, and Roxane*, as well as *Agouron*. Due to the generosity of our sponsors, HEPP News is able to be the only independent newsletter available to correctional health care providers caring for HIV-infected prison and jail inmates.

## WEB RESOURCES

**Office for Human Research Protections (OHRP)** (formerly Office for Protection from Research Risk, OPRR)  
<http://ohrp.osophs.dhhs.gov/>

**HIV/AIDS SITES:**  
**CDC AIDS Clearinghouse**  
[www.cdcnpin.org](http://www.cdcnpin.org)

**DHHS Treatment Guidelines**  
[www.hivatis.org](http://www.hivatis.org)

**HIV and Hepatitis**  
[www.hivandhepatitis.org](http://www.hivandhepatitis.org)

**HIV InSite**  
[www.ucsf.edu/medical](http://www.ucsf.edu/medical)

**Johns Hopkins AIDS**  
<http://hopkins-aids.edu>

**Medscape**  
<http://medscape.com>

**HUMAN SUBJECT RESEARCH SITES:**  
**OHRP: Prisoners as Subjects**  
<http://ohrp.osophs.dhhs.gov/humansubjects/guidance/prison.htm>  
<http://ohrp.osophs.dhhs.gov/polasur.htm>

**The New England Journal of Medicine --  
September 14, 2000 -- Vol. 343, No. 11  
Protecting Research Subjects -- What Must  
Be Done**  
[www.nejm.org/content/2000/0343/0011/0808.asp](http://www.nejm.org/content/2000/0343/0011/0808.asp)

**SELF-ASSESSMENT TEST FOR CONTINUING MEDICAL EDUCATION CREDIT**

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 Dec. 31, 2000. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Which of the following combinations would be appropriate for starting a treatment-naïve patient on ART?
  - a) Stavudine (d4T) + abacavir (ABC) + nelfinavir (NFV)
  - b) Zidovudine (ZDV) + didanosine (ddl) + nelfinavir (NFV)
  - c) Stavudine (d4T) + abacavir (ABC) + efavirenz (EFV) (in a setting with an excellent medications administration system)
  - d) All of the Above
  - e) None of the Above
  
2. Which of the following statements is false?
  - a) Pre-trial detainees have a legal right to health care because of the "due-process" clause of the 14th Amendment.
  - b) According to Supreme Court case law, prison officials are responsible for providing "adequate food, clothing, shelter, and medical care."
  - c) Circuit and district courts have uniformly interpreted "adequate...medical care" to include access to Protease Inhibitors.
  
3. In which of the following settings has Kaletra (lopinavir-ritonavir) been shown to be successful?
  - a) In treatment-naïve patients
  - b) In salvage regimens where the patient was failing NNRTIs.
  - c) In salvage regimens where the patient was failing 2 PIs.
  - d) A and C
  - e) All of the above.
  
4. Which of the following statements is false?
  - a) Between 1998 and 1999, over half of the HIV deaths at one facility in California were due to liver disease, cardiovascular disease, cancer, accidents, and other etiologies not directly related to HIV.
  - b) New data shows that strains of HIV with multiple PI resistance mutations are often less fit and therefore less able to damage the immune system. In patients who are failing therapy but tolerating the regimen without side effects, clinicians may want to continue the same PI-regimen.
  - c) Anti-CMV treatment should be restarted presumptively in those HIV patients whose CD4 was above 300/ mm3 but has declined to <50/mm3.
  - d) All of the above
  - e) None of the above

5. Efavirenz decreases the concentration of which of the following PIs sufficiently to raise concerns about sub-therapeutic PI levels?
  - a) Indinavir
  - b) Lopinavir
  - c) Amprenavir
  - d) All of the above
  - e) None of the above. EFV has no such effect.
  
6. According to data presented at ICAAC, which of the following statements about HPV in HIV-infected persons is false?
  - a) They are more commonly infected with HPV.
  - b) They are on average infected with more serotypes of HPV
  - c) Their risk for invasive disease is not directly related to the decline in CD4 count.
  - d) They have a greater incidence of clinically evident HPV disease.
  - e) They are more likely to have persistent HPV infection compared to those who are not HIV infected.

**HEPP NEWS EVALUATION**

5 *Excellent* 4 *Very Good* 3 *Fair* 2 *Poor* 1 *Very Poor*

1. Please evaluate the following sections with respect to:		
	educational value	clarity
Main Article	5 4 3 2 1	5 4 3 2 1
HIV 101	5 4 3 2 1	5 4 3 2 1
Ask the Expert	5 4 3 2 1	5 4 3 2 1
Save the Dates	5 4 3 2 1	5 4 3 2 1

2. Do you feel that HEPP News helps you in your work? Why or why not?
  
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