1999

HEPP News, Vol. 2 No. 4

HIV Education Prison Project

HEPP News is sponsored by the Brown University School of Medicine Office of Continuing Medical Education and the Brown University AIDS Program

HIV Hepp Education Prison Project News

APRIL 1999 • VOLUME 2, ISSUE 4

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About HEPP

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.

Faculty Disclosure

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 beneath the authors' names.

Hepp News is supported by an unrestricted educational grant from Agouron Pharmaceuticals and we gratefully acknowledge their support.

Report from the 6th Conference on Retroviruses and Opportunistic Infections

Update from Chicago, Jan 31-Feb 3 1999

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Brown University School of Medicine

How many of the talks and posters presented at the 6th Conference on Retroviruses and Opportunistic Infections dealt directly with prisons? Very few! However, many of the presentations reported on new drugs and described new insights in the immunopathogenesis of HIV, both topics that are relevant to the management of HIV-infected patients in corrections.

The two predominant conference themes were "this is the era of drug resistance" and "improved T cell function due to HAART has not led to the eradication of the virus." Despite the lack of landmark changes in antiretroviral therapy, the good news is that for those who have access to them, current therapies continue to work.

• Origin of HIV

Researchers from the University of Alabama opened the conference with a report on the origin of HIV-1. New evidence suggests that HIV is derived from human contact with chimpanzees in West Africa, who are infected with a strain of retrovirus similar to HIV. This presentation was the first to demonstrate homology in the virus from chimpanzees, geographic endemnicity and a plausible mechanism of transmission from animal to human through the chimpanzee meat trade.

• Era of Drug Resistant HIV

Dr. Stefano Vella presented a discussion of "Antiretroviral Therapy in Adults," which focused on the emergence of resistance and salvage therapy. This reflected a growing concern among HIV providers about treating drug-resistant HIV. Dr. Vella reviewed retrospective studies of the genotyping and phenotyping assays that demonstrated the value of these new tools in the management of HIV resistance. Adding a cautionary note, he suggested that prospective clinical studies of genotyping and phenotyping will be required before we can determine whether clinicians can effectively use these tools to improve patient care. Notably, he warned against over-reliance on genotyping and phenotyping. This is because a viral provirus that is integrated into host DNA in latently infected cells may be a source of "archived" resistance to treatment, which may not be detected by these techniques (Abstract L1).

Others presented additional data on 153 patients who failed a protease containing regimen. They were randomized to management using either Genotypic Antiretroviral Resistance Testing (GART) or standard of care using routine clinical history. Patients randomized to GART were two-times more likely to become non-detectable than those whose management relied on routine clinical history (50% vs. 23% in the GART vs. Non-GART treatment arms). It appears that use of viral resistance testing will soon become part of standard clinical practice once standardization has been achieved (Abstract LB8).

In other words, those of us providing clinical care to HIV-infected inmates will need to learn the proper use of these assays. GART will soon be part of the standard of care, however this will not supplant the need to elicit an accurate and detailed medication history from our patients. GART will complement our clinical

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LETTER FROM THE EDITOR

Dear colleagues and friends,

The evolution of HIV treatment these days seems to occur faster than Darwin could have transcribed it. With each new medical conference, management of HIV becomes more interesting, complex and challenging. In this issue, my colleague and co-editor Anne De Groot M.D. summarizes the most salient components of new HIV research from the 6th Conference on Retroviruses and Opportunistic Infections, held in Chicago in early February.

The most disappointing conference news was that mathematical models now estimate that HIV eradication will take as many as 23 years, using existing HAART regimens. The good news, however, is that for those who take the medication, HAART remains effective and durable. Moreover, scientists are now exploring ways to purge HIV from latent reservoirs using cytokines such as Interleukin-2 and removing excess viral particles using plasma apheresis. Though some of the most stimulating science in the area of HIV immunopathogenesis does not have direct clinical applicability now, it was only a few short years ago when quantification of HIV (viral load determinations), development of protease inhibitors and the mathematical modeling of HIV replication and eradication seemed theoretical.

In this month's issue of HEPP News we also provide some preliminary thoughts on the use of abacavir (ABC) in corrections. Many physicians fear its use in a correctional setting because of the potential for Abacavir Hypersensitivity Syndrome. This consideration, however, must be balanced with its outstanding potency. We recommend training all correctional health staff about this problem, especially those who provide direct clinical care. This month's HIV 101 and HEPPigram further explore the use of abacavir and provide assistance with the diagnosis and management of this syndrome.

Lastly, our Ask the Experts deals with a commonly encountered problem in the correctional setting: patients who have received sequential monotherapy and may have multi-drug resistant HIV. These are tough and challenging cases and require the knowledge of an experienced HIV specialist. Moreover, it points out to us that the era of genotypic testing is upon us. Future issues of HEPP News will help elucidate the maze of genotypic and phenotypic antiretroviral resistance testing. After reading this issue, readers should understand how to manage abacavir hypersensitivity, monitor viral load and know the latest updates about HIV antiretroviral development.

Next month we'll continue our update on the Chicago Retrovirus Conference with reports on HIV care utilization, new information on gender and viral load, insights on the changing epidemiology of HIV and the impact of these reports on HIV care in the correctional setting. In the meantime, please take a moment to write to us and tell us how our content and focus work for you.

Sincerely,
Rick Altice MD
Frederick L. Altice, M.D.

Resources

TELEPHONE NUMBERS:

PEP Registry:
888.737.4448

National Clinicians' PEP Hotline:
888.448.4911

AIDS Treatment Data Network:
800.734.7104

National HIV Telephone Consultation Service:
800.933.3413

CDC National AIDS Hotline (24 hours):
800.342.AIDS

WEBSITES:

AIDS Treatment Data Network
http://204.179.124.69/network

The Body: An AIDS Information Resource
http://www.thebody.com

The Corrections Connection
http://www.corrections.com

Immunet and AIDS Treatment News
http://www.aids.org

International Association of Physicians in AIDS Care (IAPAC)
http://www.iapac.org

JAMA (Journal of the American Medical Association) HIV/AIDS Information Center
http://www.ama-assn.org/special/hiv

Johns Hopkins AIDS Service
http://www.hopkins-AIDS.edu

Medscape HIV/AIDS
http://hiv.medscape.com/Home/Topics/AIDS/AIDS.html

HIV/AIDS Treatment Service
http://www.hivatis.org/

1999 Chicago Conference on Retroviruses and Opportunitstic Infections
http://www.retroconference.org/99/

HEPP News is published twelve times a year by the Brown University AIDS Program
tel: 401.863.1725 • *e-mail:* brunap@brown.edu • www.hivcorrections.org
If you have any problems with this fax transmission please call 800-779-7051

The 6th Conference on Retroviruses and Opportunistic Infections

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history to optimize therapy for HIV-infected patients.

• New Drugs, New Combinations

A number of speakers presented new approaches to HIV treatment that are in development. Fusion inhibitors are an exciting new product of basic research on the mechanics of HIV-1 fusion into T cells. Drugs that fall in this new class include chemokine receptor blockers and nucleocapsid inhibitors. One such drug, developed by Triangel Pharmaceuticals, is in phase I trials. *In vitro* studies of this drug were presented, showing that the new drug reduces the ability of the virus to infect new target cells (Abstract 616). Other similar drugs were presented in a session devoted to HIV treatment. This type of entry-blocking drug is unlikely to supplant current therapies, however it may be complementary once patients have been adequately suppressed using existing or new antiretrovirals.

One notable new concept was "single class triple therapy," also known as protease-sparing HAART. Three nucleoside reverse transcriptase inhibitors (NRTIs) are used instead of a protease - or non-nucleoside reverse transcriptase inhibitor (NNRTI) - inclusive regimen to treat HIV. This approach limits a patient's exposure to more than one class of HIV agents, thus reserving other agents for later (hence the term protease-sparing). A French group reported on the combination of D4T/DDI/3TC vs. D4T/DDI/Nevirapine and D4T/DDI/Indinavir. The regimens were essentially equivalent in patients with early HIV disease (Abstract 18). In another study, patients administered AZT/3TC/ABC suppressed their viral loads equally as well at 24 weeks as those on standard combination regimen, AZT/3TC/Indinavir (For more information on abacavir (ABC), see HIV 101.). The study's limitation is that insufficient data were available for patients with high viral loads, and until such are available, the use of ABC as part of a triple nucleoside analogue combination should be initiated with caution for those with high viral loads or more advanced HIV disease.

The conference also included interesting new pharmacokinetic data on the use of the combination of indinavir with ritonavir. The use of 100mg of ritonavir combined with 800mg of indinavir administered twice daily led to an excellent pharmacokinetic profile that was not affected by the administration of food. Current clinical studies will evaluate the efficacy of this combination versus ritonavir 400mg with indinavir 800mg in twice daily regimens. These dosing regimens are good news for corrections.

Safety and efficacy data were presented on two new protease inhibitors, amprenavir and ABT378 combined with RTV. Both had excellent safety and tolerability profiles (amprenavir is now available through compassionate use protocols). In a dosing study of ritonavir with ABT378 (in combination with D4T+3TC among antiretroviral naive patients), 93% achieved a VL<400 copies/mL among a group of patients with a mean baseline CD4 of 400 and VL of 100,000 copies/mL (Abstract 15).

Also highlighted was a potent, second generation protease inhibitor (AG1776), in development by Agouron Pharmaceuticals, that has excellent *in vivo* activity against many high level resistant strains of HIV with multiple mutations to existing protease inhibitors (Abstract 11). Agouron and DuPont Pharma presented data regarding three different second generation NNRTIs: DMP 961, DMP 963 (Abstract 13) and AG1549 (Abstract 12). These agents had excellent bioavailability and antiviral activity. HIV-1 isolates resistant to current NNRTIs were sensitive to these new agents. The number of mutations associated with the development of resistance was correlated with cross-resistance to these new agents. Again this supports the need to change treatment early when resistance is first detected.

• HIV Eradication Pushed Into the Future

Several speakers made reference to new HIV eradication time estimates. According to current estimates, based on our new understanding of latent reservoirs of HIV, the time it will take to eradicate HIV with HAART has increased from 18 months to 23 years. Clearly, more intensive approaches to treatment are required. Hope, however, should not be forsaken, provided these reassurances: 1) the total size of the HIV reservoir after HAART is thought to be small; 2) the latent reservoir may contain drug sensitive virus if treatment is initiated early and suppression of viral load is rapid; and 3) it is possible that additional decay in infection may become evident later with more potent antiretroviral regimens. Furthermore, new methods of activating and deleting latent virus using immunomodulators such as IL-2 demonstrate early success among patients with undetectable virus. Finally, as in the case of latent tuberculosis infection, elimination may not be totally necessary if immune control is adequate.

The relevance of these discussions to correctional HIV care are clear: we need to enable our patients to adapt to a lifetime of antiretroviral medication and select treatment regimens that are highly effective from the outset and that patients can adhere to. By meeting these goals, we will have patients who are living longer and are eligible for more aggressive therapeutic options in the future.

• Adherence

Adherence remains the cornerstone of effective antiretroviral therapy both for clinical trials and for clinical efficacy. It was demonstrated that adherence can be outstanding even among homeless patients. Much of the presented science described methods to measure adherence. While electronic devices were useful in monitoring adherence - although once thought to be the gold standard - they can be problematic. The bottom line is: develop effective ways for patients in corrections to have easy medication access and teach them effective mechanisms for taking pills. The pharmaceutical industry still has a long way to go in developing more user-friendly regimens for corrections.

• Effect of HAART on Immune Response

Several abstracts presented data on the recovery of effective T lymphocyte responses among patients with advanced HIV who achieved virologic success using HAART. Although patients successfully responding to HAART may not always redevelop T lymphocyte responses to HIV, several studies demonstrated renewed responses to CMV, toxoplasmosis and MAC as well as other neo-antigens. Poor restoration of these responses was correlated with risk for relapse of opportunistic infections and/or new opportunistic infections (OI) among at-risk patients treated with HAART. These data suggest that for some patients, prophylaxis may be stopped, but we do not yet have access to the types of tools that would assist us with these difficult decisions (Abstract 453-7).

The timing of HAART initiation appeared to be a determinant of the recovery of responses to HIV antigens. Late treatment had some effect, but recovery of anti-HIV and anti-OI immune responses was less complete than among patients who were treated with effective antiretroviral therapy at earlier stages. More than one presenter made the analogy that "holes in the T cell repertoire" were more difficult to fill in with new, effective T cell responses the longer one delayed initiation of HAART (Abstract 329).

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The 6th Conference on Retroviruses and Opportunistic Infections

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• Intermittent Therapy: Route to Remission?

The case of the Berlin patient was presented in a poster (Abstract 351) along with a few other cases of "controlled HIV infection." Few adults, with the exception of this example have achieved complete viral suppression with the administration of HAART. The general consensus among participants was that the type of interrupted HAART combined with immune stimulation (due to acute Hepatitis A infection) that put the Berlin patient into apparent remission is not easy to replicate in other patients. Interrupted therapy will require intensive study before it can be determined that this approach will enable some patients to completely discontinue treatment. Patients who are interested in this approach should be referred to "centers of excellence." Those of us in corrections do not have enough data to support such an approach.

• What Innovations Do We Need Now?

Looking toward the future of antiretroviral therapy, many speakers emphasized the need for new drugs with better resistance profiles and suggested that we initiate therapy with more potent regimens. Cost-intensive genotyping/phenotyping assays may need to be implemented more frequently as more patients fail their first and second lines of therapy. Studies demonstrating the prospective efficacy of these tools are needed.

HIV treatment is becoming more complicated with the emergence of resistance and the addition of new treatment regimens. The implication for corrections is that the management of HIV-infected individuals by experienced providers, and careful monitoring of patient adherence, is important if we want to pre-empt the need for greater reliance on cost-intensive assays.

• Looking Beyond the Borders

Dr. Vella said in his closing remark that most of his recommendations addressed only 10% of the global population, and that the remaining 90% of people in the world who have no access to treatment should be considered. To place the problem of access to HIV care in a greater context, he quoted HIV expert Paul Volberding, who said "inequitable distribution of medical resources is not unique to HIV infection. Improving health care access is a challenge that extends beyond that of the HIV epidemic." Dr. Vella need not look much farther than the closest jail or prison. Parallels between health care access problems in the developing world and our patients' access to HIV care prior to incarceration are self-evident.

Abstracts available on the web at http://www.retroconference.org/99/

**Anne De Groot, M.D., Consultant: Agouron, Bristol-Myers Squbb; Speaker's Bureau: Agouron, Bristol-Myers Squbb, Glaxo Wellcome.*

HEPPigram

A feature of HEPP News providing concise solutions to correctional HIV-related problems

Management of the Abacavir Hypersensitivity Syndrome (AHS)

1. Counsel patients about the risk and symptoms of this syndrome prior to starting therapy. Consider Abacavir Hypersensitivity Syndrome (AHS) if the patient is within six weeks of initiating abacavir (ABC) and has a skin rash or two or more of the following sets of symptoms that persist and progress beyond 72 to 96 hours:
   - fever
   - nausea, vomiting, diarrhea or abdominal pain
   - myalgias, severe fatigue or malaise

2. Make sure patients are instructed to contact medical staff immediately if symptoms occur within the first six weeks of starting ABC. Also counsel them NOT to discontinue medications themselves. Doing so would confuse later decision-making.

3. If symptoms develop, evaluate the patient immediately. Evaluation should include blood pressure, examination for rash, chemistry profile and CBC. Symptoms may be indistinguishable from a viral syndrome, however they usually do not include respiratory complaints.

4. Arrange to see the patient DAILY for the next 72 hours after symptoms begin. In some cases, admission to the medical infirmary may be indicated. Do NOT discontinue ABC at this time. If nausea or vomiting is an important component of the patient's symptoms, prescribe antiemetics to ensure that the patient can continue to take his/her medication.

5. If the patient has a viral syndrome, the symptoms should abate within 72 to 96 hours. If the symptoms progress or do not remit, AHS should be considered at that point and the ABC should be stopped. The AHS should not be life threatening if diagnosed early.

6. If it is decided after waiting the prescribed amount of time that the patient does have the AHS (occurs in 3%-5% of patients), ABC should be discontinued. The symptoms will abate within 24 to 48 hours.

7. Once the AHS is diagnosed or suspected and medications have been discontinued, NEVER rechallenge the patient with ABC. Make sure the chart is marked as such and that the patient is counseled to never take ABC again.

8. It is important NOT to stop ABC when symptoms first appear without further investigation as described above, as they are indistinguishable from a viral syndrome. Because AHS is not dangerous if detected early, clinicians have the opportunity to follow the patient and determine if the patient's symptoms disappear. If, on the other hand, ABC is stopped before confirmation of AHS, it could preclude the use of a truly potent antiretroviral that the patient might need in the future. Unfortunately, if ABC is stopped (because of presumed but unconfirmed ASH) it can never be used again.

9. Please note that patients who stop ABC for OTHER reasons (e.g. non-adherence), CAN be restarted on ABC.

Ask The Experts

M.R. is a 42 year-old male diagnosed with HIV in 1990. He started AZT at that time when his CD4 count was 490 and took AZT monotherapy until March 1994, when he was changed to D4T monotherapy. In November 1995, his CD4 dropped to 220 and he was switched to AZT plus 3TC. In April 1996, while on AZT and 3TC, his viral load was 58,000 and his CD4 count was 190. At that time, indinavir 800 TID was added to his therapy. Within one month, his viral load decreased to 4,200 copies and he tolerated his medications well. By January 1997, after excellent adherence, but receiving his medication coincident with meals at 6 a.m., noon and 6 p.m., his viral load was 74,000 and his CD4 count was 310. At this time, his regimen was changed to D4T BID, DDI BID and NFV TID. After 4 weeks, his viral load dropped to 6,800 copies, where it remained for six more months. However, T cells had risen to 420. The patient had difficulty arriving at the medication line for his midday NFV dose and missed it approximately three times per week. He intermittently missed his medications because of diarrhea and abdominal cramping. By December 1997, the viral load had increased to 43,000 and nevirapine was added to his regimen. He has remained on nevirapine and, despite an initial increase in his CD4 count, his viral load is now 168,000 and his CD4 count is down to 260. What is the next regimen and what would you use?

What Would You Do?

Expert 1: David Thomas, M.D.
Medical Director, Florida Department of Corrections, Tallahassee, FL
Consultant: Agouron, Bristol-Myers Squibb;
Speaker's Bureau: Agouron, Bristol-Myers Squibb.

Unfortunately, this case is common in the prison setting and involves sequential monotherapy that, as we have learned, is an undesirable treatment strategy. I would not treat this patient without first obtaining a genotypic antiretroviral resistance test. Patients may fail therapy because of development of resistance, non-adherence, malabsorption or pharmacokinetic interactions. For four years he was on monotherapy with either AZT or D4T. For his fifth year, he was placed on progressive monotherapy with either 3TC (added to AZT) or a protease inhibitor.

It is clear that the progressive monotherapy use of indinavir in April 1996, an extremely commonplace practice then, led to virologic failure despite an impressive T cell response - this VL and CD4 paradox is a recent phenomena of intense interest. The interaction with food is probably a red herring. However, if inadequate drug bioavailability occurred, virological failure has been reported and is not related to the development of genotypic mutations.

Having been on all classes of existing drugs in 1997, genotyping is essential. He is likely to have developed the M184V mutation associated with 3TC resistance. If he has this mutation without other associated NRTI mutations, there would be a 4-fold decrease in the efficacy of abacavir, which could then be used. If other NRTI mutations exist, there would be expected little or no response to ABC. Alternatively, the use of adefovir, a nucleotide analogue RTI available by compassionate use, is likely to achieve a 1.0 log reduction in the presence of the M184V mutation.

If there is no 103 or 181 mutation associated with resistance to the class of NNRTIs, then efavirenz (EFV) may be effective. It is critical to know the protease mutation sites for the selection of a PI. If there is no mutation at the 90 codon, saquinavir-SGC may be of some use. Alternatively, if the indinavir failed because of poor absorption and a lack of an 82 or 84 mutation exists (associated with resistance to RTV or IDV), the combination of RTV/SQV would be effective.

If genotyping is not available for this patient, the best blind regimen would probably be EFV, saquinavir-SGC, RTV and adefovir. Genotyping would give the prescribing physician comfort in selecting the most appropriate proteases. It would also reveal a possibility for a NRTI, which may make a difference in this salvage regimen. For instance, DDI could be resalvaged with the use of hydroxyurea.

Recent data from Zolopa from the 12th International AIDS Conference demonstrated that in patients who were failing a protease containing regimen, that genotypic assays with expert advice were better predictors of a successful outcome than other clinical or antiretroviral drug history predictors. This was based on a study of 80 patients, 30% of whom became undetectable using genotype-driven therapy as opposed to 17% of those in a standard arm.

Unfortunately, there is considerable variability in the quality of available genotypic assays. I would make sure I was using a reputable company and base my decisions on the clinical drug history and the genotypic findings. This patient teaches us much about the natural history of modern antiretroviral therapy and the consequences of inadequate therapy at initiation. Today, newly diagnosed patients have better opportunities for achieving virological success.

Expert 2: Joe Bick, M.D.
Chief Medical Officer,
HIV Treatment, California Medical Facility, Vacaville, CA
Speaker's Bureau: Agouron, Bristol-Myers Squibb.

Although the past several years have brought encouraging new treatment options for antiretroviral therapy (ART) naive patients, this man is more representative of the typical patient encountered in our correctional practices. Through the early and mid-part of this decade, most patients were treated with the sequential addition or substitution of one agent at a time. We now know that this practice is a sure recipe for the rapid development of multidrug resistant HIV.

During four years of AZT monotherapy followed by 18 months of D4T alone, it is likely that significant resistance to both agents developed. Therefore, switching to the combination of AZT/3TC probably represented adding a single agent to a resistant regimen, as did adding indinavir five months later.

In spite of broad cross resistance among protease inhibitors, this patient achieved ~ 1 log reduction in his HIV VL by the new regimen. Unfortunately, his adherence was suboptimal. New adherence data has shown that missing more than 5% of ART doses (1-2 days worth per month) leads to a dramatic decline in the percentage of patients who achieve an undetectable HIV viral load. (1) Clearly, this patient did not achieve that threshold.

Should we simply select three or four agents that the patient hasn't had before for a salvage regimen? Data from the genotypic antiretroviral resistance study (GART) demonstrated that outcomes (as measured by achieving an undetectable HIV viral load) are significantly better when treatment decisions are made based upon genotypic analysis and "expert opinion," as opposed to treatment history alone. (2) Although improvements are needed in resistance assays, they can provide useful information especially in the setting of heavily pretreated suboptimally adherent patients. Thus far, genotyping predicts what will not work better than what will.

This patient has not yet received ritonavir, saquinavir, abacavir, or efavirenz. However, his prior indinavir and nelfinavir exposure may have led to mutations that will decrease the efficacy of ritonavir and/or saquinavir (82, 84, 90). If his virus is resistant to 3 or more nucleoside RTIs, it is less likely that abacavir will be effective. If his nevirapine exposure led to a 103 mutation, it is unlikely that efavirenz will be useful. For these reasons, genotyping may be helpful in determining if there is a chance that previously used agents are still viable treatment options.

Genotyping can cost as much as $600 depending on the laboratory contract. On the other hand, triple therapy costs at least $250 per week; in this patient, at least four drugs may be required costing even more! Rather than initiating an ineffective regimen and then checking a viral load 4 to 6 weeks later (>$800-$1,500), the use of a genotypic assay may be cost effective.

Whatever regimen is chosen, a crucial factor in this patient's eventual treatment success or failure is time spent on education and preparation. An effective peer education program can assist in maximizing adherence. Attention spent on preparing the patient for and treating any side effects is also very important. The next regimen may well be the only one available for the foreseeable future, so it must be selected with the utmost care.

1) Paterson et al, 6th Conference on Retroviruses and Opportunistic Infections. Chicago (IL) 1999. Abstract 92.
2) Baxter et al, 6th Conference on Opportunistic Infections. Chicago (IL) 1999. Abstract 8.

HIV 101

Abacavir

This month we are providing a treatment update on the use of abacavir, a new and most potent NRTI, in corrections. Recent data using abacavir (ABC, Ziagen®) as part of a protease-sparing regimen has provided early data to suggest its efficacy for certain groups of individuals infected with HIV. Despite these findings, the most recent guidelines have not assisted clinicians on its appropriate use. In this article, we intend to provide an overview of this new nucleoside analogue and insight into its appropriate use, possible side effects, and management in the correctional system.

In prospective clinical trials abacavir has been effectively combined with ZDV and 3TC among patients with relatively high CD4 lymphocyte counts (Mean CD4≅450). After 48 weeks of therapy and with near similar results as found in triple combinations using a protease inhibitor, the proportion who achieved a viral load (VL) of <400 copies/mL was 65%. Due to the use of more sensitive assays (VL < 50 copies/ml), variable results were found among those achieving non-detectable status when stratifying by baseline HIV-1 RNA level (see this month's News Flashes for more information on this assay). Only 28% of those with baseline VL >100,000 copies/mL achieved successful suppression of viral load below detectable limits. Abacavir's use in nucleoside-only combinations should probably be reserved for patients with lower baseline viral loads. ABC will also be most effective when used by patients who have not been heavily pre-treated with nucleoside analogues. Further information on studies related to this new drug will be included in the May HEPP News.

Thus, the best use of ABC's potency is for nucleoside-naive patients, patients with newly detected antiretroviral failure where multiple mutations are less likely, or as part of intensification regimens for patients who do not achieve <1000 copies/mL after 4 weeks or <50 copies after 6 months of initiation of therapy. Though official guidelines do not exist for the use of ABC, the following recommendations are based on what we know about the potency of currently recommended antiretrovirals as well as current pathogenesis information. Three potential clinical scenarios for the use of ABC in combination antiretroviral therapy are listed in the ***table below.***

Clinical Scenarios for the Possible Use of Abacavir (ABC)

Antiretroviral Naive Patients:	**Antiretroviral Experienced Patients:**	**Antiretroviral Intensification:**
a) For patients at any stage of HIV infection, consider combining with ZDV or D4T (thymidine analogues) plus either a potent protease inhibitor or efavirenz b) For patients with non-advanced HIV (CD4>200 and VL<100,000), consider using ABC as part of a protease-sparing regimen when combined with: • ZDV+DDI • D4T+DDI • ZDV+DDC • ZDV+3TC • D4T+3TC	a) Use as part of the first salvage regimen when possible b) Use as part of a salvage regimen before the viral load rebounds to high levels when multiple mutations may develop c) When possible, obtain a genotypic assay to determine the number of mutations present to guide ABC's use	Consider adding ABC to a potent three drug regimen when early predictors are present: a) VL is >1000 copies/mL four weeks after initiating triple combination therapy b) VL is >50 copies/mL six months after initiating triple combination therapy c) Do not add ABC as a single agent to a failing regimen

Advantages of ABC are that it does not require nor interfere with P450 enzymes for metabolism, it is the only nucleoside analogue that is not principally cleared renally and is well-tolerated by most patients. With the exception of mild hyperglycemia, ABC has only one major adverse side effect that must be a concern for correctional physicians and health staff administering ABC. Abacavir Hypersensitivity Syndrome (AHS) occurs in approximately 3-5% of patients and must be taken very seriously. All definite and most possible cases of this adverse event occur within the first 6 weeks of therapy. AHS typically begins with nausea, vomiting, myalgias, fever, and sometimes rash. Symptoms become progressive over several days to weeks. Death has not occurred in patients with this syndrome who were discontinued within the first week of onset of symptoms. These symptoms are similar to many viral syndromes with a serum-sickness-like presentation. Unlike a viral syndrome, the AHS will persist beyond 72 hours. This syndrome disappears promptly after discontinuation of the medication.

While the syndrome, during its initial presentation has not been associated with significant morbidity or mortality if diagnosed within a week of onset of symptoms, rechallenge with ABC has resulted in hospitalization and even death secondary to hypotension. Therefore, among patients who develop a "viral-like" syndrome within the first 6 weeks of therapy, patients must be monitored daily until symptoms either abate or progress beyond 72-96 hours (See HEPPigram on pg. 4).

Thus, ABC provides an effective new agent for the management of HIV, however, correctional staff must develop a system for managing problems and must be adequately taught about the use and consequences of ABC. Hopefully, this review will give more correctional staff confidence in its future use.

News Flashes

▶ **February, 1999**

New York State Department of Corrections Report Released

The New York AIDS Advisory Council released a report on the New York State Department of Corrections (NYS DOC). The report was a result of a project that began ten years ago when the AIDS Advisory Council initially reported serious deficiencies in prison health services, particularly for inmates with HIV. At that time, the council recommended immediate steps for improvement, and suggested that failure to accomplish the changes within 18 months should result in transfer of authority for inmate health services to the Department of Health. The February 1999 report by the New York AIDS Advisory Council again listed many problems with HIV care in the state's correctional facilities, relating to access to HIV care, transfer of records and access to HIV testing, counseling, and education. To obtain a copy of the report, contact the New York State AIDS Institute at 518.473.2903.

The Council's report contradicts, in part, a recent report showing a decline in the number of AIDS deaths within the New York correctional facilities which is most likely due to providing inmates with increased access to standard antiretroviral treatments and medications for the prevention of opportunistic infections. (MMWR Jan. 8, 1999; 47(51&52) 1115. http://www.cdc.gov/epo/mmwr/mmwr.html).

▶ **March 3, 1999**

Ultrasensitive Viral Load Assay Test Approved

The U.S. FDA recently approved Roche's Amplicor Ultrasensitive viral load test. This assay accurately measures levels of HIV to as low as 50 copies/mL, but is not accurate above 50,000 copies/mL. This means we have a new lower limit for "undetectable." Recent studies have indicated that a viral load below 50 copies/ml is associated with a more complete and durable viral suppression. Using this test, providers will be able to monitor more closely the effectiveness of HAART. The cost to laboratories to perform this new ultrasensitive test is the same as for the older assay. For more information on this test or Roche's patient assistance program, call 1-888-837-8727.

▶ **March 7 and 15, 1999**

Increased Drug Arrests, Climbing Inmate Population

Two articles in the New York Times reported on statistics that the Bureau of Justice Statistics recently released about prison populations. The report found that there were 1.8 million inmates incarcerated in the United States last year (1,277,866 state and Federal inmates, an increase of 4.8 percent; and 592,462 city and county jail inmates, an increase of 4.5 percent). Experts say increases in prison and jail populations reflect tougher sentencing laws, longer sentences and tougher parole boards, and imply that prosecutors and judges are being more stringent.

Drug offenses accounted for the greatest share of the increase in state prisoners - almost 30% of crimes committed from 1980 to 1996. Drug-related crimes are not included in the Federal Bureau of Investigation's calculation of the national crime rate. Thus, increasing rates of drug-related crimes are responsible, for the major part, for increases in prison populations. This information contrasts with popular belief that incarceration rates are inversely correlated with crime rates.

The overall number of inmates has doubled since 1985, with no signs of stopping. Rates of HIV infection among inmates are also unlikely to decline very rapidly in correctional settings, due to increases in the number of individuals who are arrested for drug-related crimes. See the New York Times website for the complete text of the articles: www.nytimes.com. For more updated statistics, look at the Bureau of Justice Statistics website: www.ojp.usdoj.gov/bjs/whtsnw2.htm.

Save The Dates

9th Annual Clinical Care of the Patient with HIV Infection
April 12 - 13, 1999, Baltimore, MD
This course will provide a state-of-the-art overview of the clinical care of HIV+ patients for practicing clinicians and other health professionals.
Sponsored by: Johns Hopkins University, School of Medicine, CME
Contact: Office of CME, Johns Hopkins University, School of Medicine,
tel: (410) 955-2959, fax: (410) 955-0807
email: cmenet@som.adm.jhu.edu. web: www.med.jhu.edu/cme.

HIV Update: Contemporary Issues in Management
May 2-4, 1999, Boston, MA
Harvard Medical Schools
Beth Israel Deaconess Medical Center
Contact: Professional Meeting Planners
tel: 781.279.9887, 1.800.378.6857
fax: 781.279.9875 email: PMPMeeting@aol.com

International AIDS Society
USA HIV Management Updates
April 12, 1999, San Francisco, CA
April 21, 1999, Chicago, IL
May 8, 1999, Cleveland, OH
This program, now in its seventh year, reviews the most recent developments in the field of HIV disease pathogenesis and antiretroviral management. Expert faculty will speak on timely and clinically relevant issues in the management of HIV disease.
Topics include improving the management of HIV disease, HIV pathogenesis, antiretroviralas and other selected issues in HIV disease management.
Contact: International AIDS Society--USA
tel: 415.561.6725
fax: 415.561.6740
e-mail: cme@iasusa.org

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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 June 15, 1999. The estimated time for completion of this activity is one hour and there is no fee for participation in this activity.

1. Which of the following is true about the use of abacavir?
   a. it is the most potent nucleoside analogue reverse transcriptase inhibitor
   b. it is unlikely to be effective as salvage therapy in patients who have multiple mutations to zidovudine and a single mutation to lamivudine
   c. can be an important component of both protease-sparing and protease-containing antiretroviral regimens
   d. a and c only
   e. a, b and c above

2. The Food and Drug Administration (FDA) has recently approved use of an ultrasensitive viral load assay that measures HIV-1 RNA copies from between 50 copies/mL and 50,000 copies/mL.
   a. True b. False

3. Which is FALSE about the Abacavir Hypersensitivity Syndrome?
   a. it usually occurs within the first six weeks after initiating abacavir
   b. usually consists of nausea, vomiting, fevers, myalgias and, sometimes rash
   c. may be lethal if the medication is not stopped within one week during the initial course of abacavir
   d. may be lethal if a patient is rechallenged with abacavir after the syndrome has developed
   e. the syndrome disappears promptly after discontinuing the medication

4. Which of the following statements about managing HIV is incorrect?
   a. HIV may take as long as 23 years to eradicate using existing antiretroviral therapy
   b. genotypic antiretroviral resistance testing is more predictive of a virologic success than a standard antiretroviral drug history
   c. chemokines like Interleukin-2 promote viral replication and may expedite eradication of HIV from existing reservoirs
   d. the standard viral load assay is more useful to use to assess prognosis, whereas the new ultrasensitive assay is best used to evaluate response to antiretroviral therapy
   e. abacavir should be used to initiate therapy when the viral load is greater than 100,000

5. A patient who was successfully on an abacavir-containing regimen for four months was released from prison, however was unable to afford medication after release and was on no antiretroviral therapy when he was reincarcerated two months later. Upon return to prison, the patient can safely be restarted on ABC (as part of a potent combination).
   a. True b. False

HEPP News Evaluation

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