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HEPP REPORT

March 2003 Vol. 6, Issue 3

HIV & HEPATITIS
EDUCATION
PRISON
PROJECT

INFECTIOUS DISEASES IN CORRECTIONS

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ABOUT HEPP

HEPP Report, a forum for correctional problem solving, targets correctional administrators and HIV/AIDS and hepatitis care providers including physicians, nurses, outreach workers, and case managers. Published monthly and distributed by email and fax, HEPP Report provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, and efficient approaches to administering treatment in the correctional environment. 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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REPORT FROM THE 10TH CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS

By David Alain Wohl, M.D., The University of North Carolina

Note: This article contains discussion of off-label use of some drugs; not all have been approved for that use by the FDA.

The Conference on Retroviruses and Opportunistic Infections (CROI), despite its awkward and outmoded name, has become the most important venue for the dissemination of results from HIV-related research in the U.S. and, arguably, the world. The 10th CROI held in Boston on February 10-14 was more clinically oriented than most of the preceding conferences and saw results from several important clinical trials presented, as well as preliminary data from studies of new antiretroviral agents and updates on the epidemiology of the epidemic.

CLINICAL TRIAL RESULTS 2NN Study

A presentation of the large Boehringer Ingelheim-sponsored 2NN Study¹ by International AIDS Society President Joep Lange was of key interest to many attending the conference. These long-awaited results detailed the efficacy and safety of initial antiretroviral therapy with stavudine (d4T) and lamivudine (3TC), plus one of the following:

- ♦ nevirapine (NVP) 400 mg QD,
- ♦ NVP 200 mg BID,
- ♦ efavirenz (EFV) 600 QD, or
- ♦ a combination of NVP 400 mg QD + EFV 800 mg QD

A total of 1,216 subjects enrolled in 17 countries. All subjects were treatment naïve; median HIV viral load and CD4+ cell count were 4.7 log₁₀ copies/mL (~50,000 copies/mL) and 109/uL, respectively. Treatment failure was defined as less than a 1 log₁₀ decline in HIV RNA level by week 12, two consecutive viral load measurements above 50 copies/mL after week 24, a new Centers for Disease Control and Prevention (CDC) category C diagnosis or death, or change of study-assigned therapy.

About 84% of subjects completed the study.

After 48 weeks, success (absence of above-defined failure) was fairly comparable across arms with 56% of the NVP QD arm, 56% of the NVP BID arm, 62% of the EFV arm and 47% of the NVP+EFV arm achieving this endpoint. A statistically significant difference was only seen between the EFV and the NVP+EFV arms. A change in treatment occurred most commonly in the dual Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) assigned subjects (34.5%), followed by NVP QD (29%) and less commonly NVP BID (22%) and EFV (20%). In an intent to treat analysis, the proportion of subjects with a viral load below 50 copies/mL at week 48 was 70% in both the NVP QD and the EFV arms, 65% in the NVP BID arm and 63% in the dual NNRTI arm. Response to treatment based on baseline viral load demonstrated a decline in treatment success rates in all the study arms when the HIV RNA level was >100,000 copies/mL at entry with a suggestion that the EFV arm tended to be superior compared to the NVP arms. CD4+ cell counts increased in all the groups not dissimilarly with approximately a 140-150 cell/uL rise experienced from baseline to week 48.

While virologic and immunologic efficacy was not wildly different among arms, adverse events did distinguish the study regimens. Overall, there was more toxicity reported in the NVP containing arms than the EFV arm. The proportion of subjects who had treatment limiting adverse events in the four arms ranged from 30% in the dual NNRTI arm to 15.5% in the EFV QD arm; 24% of the NVP QD and 21% of the NVP BID discontinued therapy dur-

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ing the study. Hepatotoxicity comprised the lion's share of grade 3 (severe) and grade 4 (life threatening) laboratory toxicity with 13.2% of the NVP QD, 7.8% of the NVP BID, 4.5% of the EFV QD and 8.6% of the dual NNRTI subjects experiencing elevations of ALT and/or AST ($p < 0.001$ NVP QD vs. EFV QD). About 10% of the cohort was HCV seropositive and 5% had active HBV infection and these patients were distributed equally across the study arms. CNS adverse events were not surprisingly significantly higher among those taking EFV (5.5% had grade 3 or 4 CNS toxicity in this arm).

During the trial, 25 people died. Eleven of these deaths were associated with HIV disease and another 11 from non-HIV or study treatment related causes (including a number of murders occurring in South Africa). In the remaining three cases, death was attributed to study medication: one died from lactic acidosis associated with d4T use, one woman developed fatal toxic hepatitis while on NVP without evidence of viral hepatitis and another man also receiving NVP developed Stevens-Johnson Syndrome and subsequent fulminate sepsis.

This long-awaited study demonstrated parity in potency between NVP and EFV and the feasibility of once daily dosing with NVP. The higher rates of serious toxicity, specifically hepatotoxicity, in the NVP arms may dampen some clinicians' enthusiasm for once a day NVP, although others may opt for this convenient alternative to EFV coupled with close monitoring of liver functions.

903 Study

Another study with implications for clinical care, the Gilead 903 Study², pitted tenofovir (TDF) against d4T as part of a three-drug regimen with 3TC and EFV in 600 antiretroviral naïve patients. In a presentation of 96-week results from this trial, the extremely high rates of viral suppression reported after 48 weeks have persisted. In both study arms the proportion of subjects with a viral load less than 50 copies/mL was between 74% and 78% - a response that is all the more impressive considering the median baseline viral load was 81,000 copies/mL and the median entry CD4+ cell count 276/mm³.

However, as in the 2NN Study, it is the toxicities that set the regimens apart. Fasting triglyceride levels rose significantly higher in the d4T+3TC+EFV arm com-

pared to those assigned to TDF+3TC+EFV (100 mg/dL vs. 5 mg/dL, $p=0.001$). Likewise, total cholesterol increased 50 mg/dL in the d4T group and 30 mg/dL in the TDF group. Reflecting these changes in lipids and indicating their clinical significance, rates of new statin and fibrate use during the study was much higher in the d4T subjects than the TDF patients (10% vs. 2%). Other metabolic complications were also compared. Investigator-defined lipodystrophy was reported in four times as many d4T subjects. Differences between limb fat at 96 weeks by DEXA scanning were also seen. Those assigned TDF had about eight pounds more peripheral fat than d4T subjects. DEXAs were also obtained longitudinally to assess bone density. These results were released after the conference and demonstrated slight declines in bone mineralization in both study arms. However, although the differences between arms were statistically significant, thus far, they are of limited clinical significance.

This important study indicates that tenofovir can hold its own against d4T in suppressing viral replication and does so with less toxicity. That the study compared two regimens that can both now be administered once daily was prescient - and certainly increases the attractiveness of the TDF regimen within corrections.

Pegylated Interferon for Early-Stage HIV

Researchers from Germany presented results of a study³ that treated early-stage HIV-positive patients with weekly injections of pegylated interferon Alfa-2b (PegIntron). Ten patients with early-stage HIV and no symptoms who had not yet received treatment were studied; five patients received weekly PegIntron injections while the other five patients received no treatment.

At baseline the average CD4 count in the group that received therapy was 462; the control group CD4 count averaged 535. After six months, the average CD4 count in the treatment group had increased to 611 while the average CD4 in the control group dropped to 450. Viral load in the group receiving therapy dropped from 22,158 copies/mL to 3,039 copies/mL. The viral load in the control group went from 7,136 copies/mL to 40,092 copies/mL.

The presenters reported no serious side effects in the treatment group, perhaps

due to the fact that the PegIntron dose was half the standard dose used for hepatitis C therapy.

This study of a small number of patients offers some intriguing data on the favorable immunologic and virologic effects of interferon therapy. Further studies are needed to assess the longer-term effects and toxicities when using interferon to treat patients with early-stage HIV infection.

**DRUG-DRUG INTERACTIONS
Tenofovir and ddl**

In addition to results of large clinical trials, several reports focused on important drug interactions of the agents currently used to treat HIV infection. As many providers know, co-administration of tenofovir and didanosine (ddl) leads to elevated plasma levels of ddl and, therefore, potential heightened risk of ddl-related toxicity. In contrast, ddl does not alter tenofovir levels. In response to the effect of tenofovir on ddl levels, clinicians have been using a reduced dose of 250 mg of ddl-EC (enteric coated) along with tenofovir.

The pharmacokinetics of this dose of ddl-EC when coupled with tenofovir in a fed and fasted state was studied⁴ in HIV-uninfected volunteers. Dosing of 250 mg ddl-EC on an empty stomach followed two hours later by 300 mg tenofovir and a light meal resulted in a ddl exposure identical to that seen when ddl-EC is administered as 400 mg by itself. Concomitant administration of 250 mg ddl-EC and tenofovir without food led to a slightly lower ddl exposure relative to 400 mg of ddl-EC (88.6% geometric mean exposure) but when the two were taken with food, ddl levels increased by 114%. Generally, these data indicate that a dose reduction of enteric-coated ddl to 250 mg is appropriate when this agent is used with tenofovir however, it should be noted that all subjects weighed over 60 kg. The differences in exposure in the various scenarios tested were not major and the convenience of being able to take both medications with a light meal has led many to recommend this dosing schedule to their patients. Appropriate dosing in those who weigh less than 60 kg is unclear and certainly requires further study.

Lopinavir/ritonavir and Phenytoin

Kashuba and colleagues examined a potential drug-drug interaction between lopinavir/ritonavir and the anticonvulsant phenytoin (Dilantin)⁵. Lopinavir/ritonavir is

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LETTER FROM THE EDITOR

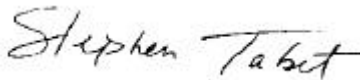
Dear Correctional Colleagues:

This issue of HEPP focuses on the 10th annual Conference on Retroviruses and Opportunistic Infections (CROI) held February 10-14 in Boston. The meeting opened with a well thought-out and charismatic speech on HIV, politics, and citizenship in the world by former President Bill Clinton. Clinton's accurate quotations of HIV statistics and grasp of the world AIDS problem was mind-boggling and inspiring. Clinton spoke of work that his own foundation is doing throughout the world to fight AIDS. He also praised President George W. Bush for pledging \$15 billion dollars to help fight AIDS in the highest prevalence countries. Clinton did caution that systems need to be in place to ensure that countries that receive funding are prepared to spend it effectively.

Since its beginning, the organizers of CROI have focused on providing a forum for scientists and clinicians to present, discuss, and critique presentations in the field of human retrovirology and opportunistic infections. The number of attendees (3,200 this year) has always been limited; most are HIV researchers and clinicians. The paucity of pharmaceutical sales representation is intentional. I, and many others, feel that CROI's restrictions are refreshing and help keep the meeting more focused. Others feel that limiting who can attend CROI is elitism by the medical and research communities at its their worst. One of my friends, a long-time AIDS activist, told me recently that while he originally had adamantly protested the strict attendance rules of CROI, he has come to understand them.

In the current issue of HEPP, Drs. Wohl and Piliero summarize several important studies presented at CROI. I attended CROI and afterward, many colleagues told me that they didn't hear much come out of this year's meeting. I was asked several times what I thought the most important study was this year. Arguably, I believe the 2NN Study presented by Joep Lange (and reviewed by Dr. Wohl in this issue of HEPP) receives that distinction. The 2NN Study provides further evidence that efavirenz is not more potent than nevirapine leaving us with two powerful NNRTI options - each with their own set of positive and negative aspects.

After reading this month's issue, you should be familiar with some of the data presented during the 10th annual Conference on Retroviruses and Opportunistic Infections, including the 2NN Study, the 903 Study, the D:A:D Study, and several new antiretroviral therapies, among others.



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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 at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV and hepatitis unless otherwise indicated. For the treatment of HIV and hepatitis infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

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an inhibitor of CYP3A4 and, like phenytoin, a CYP450 inducer. Phenytoin is a substrate for CYP2C9 and CYP2C19. To investigate the interactions between these agents, 24 HIV-uninfected volunteers were randomized to two groups, the first of which received lopinavir/ritonavir 400 mg BID for 10 days followed by concomitant administration of the PI with 300 mg QD of phenytoin for 12 more days. The other arm started the study taking phenytoin alone and then added lopinavir/ritonavir at day 11 through day 22. Intensive pharmacokinetics were performed and revealed a two-way interaction between these drugs in which levels of both are decreased. Clinically, this may mean that phenytoin levels may drop if lopinavir/ritonavir is added; therefore levels of the anticonvulsant should be checked soon after the PI is added. Levels of lopinavir may also drop despite the low dose ritonavir present in the formulation. Whether this reduced exposure can be compensated for by the addition of more lopinavir/ritonavir is unclear as this could lead to even greater reduction in phenytoin. Follow-up studies of the complex interactions between these drugs and possible regimen adjustments to compensate are planned.

The interactions between phenytoin and lopinavir/ritonavir are complex enough that they should be not be co-administered in the same patient.

METABOLIC COMPLICATIONS

The centerpiece of the session on metabolic complications associated with HIV was the D:A:D Study⁶, a large meta-cohort study of cardiovascular disease involving 23,468 subjects from the U.S., Europe and Australia. At baseline, participants had a median age of 39 years, 24% were women, 55% had viral loads below the limits of

assay detection, 67% were PI experienced, 34% NNRTI experienced, 20-30% had elevated total cholesterol or triglycerides and 60% were current smokers. During the study, 126 subjects had probable or definite myocardial infarctions (MIs), 28% of which were fatal. Men experienced all but 10% of the MIs. In an analysis of exposure to highly active antiretroviral therapy (combination treatment which includes a PI and/or an NNRTI plus NRTIs) and outcome of MI, there was a linear trend of increased risk of MI with greater exposure to HAART. The relative risk of MI increased by 1.26 (95% CI, 1.12-1.41) per year of HAART exposure (i.e. a 26% increased annual risk of MI). Other factors that placed participants at risk for MI included increased age, male gender, previous cardiovascular disease, smoking and elevated total cholesterol. Enigmatically, the presence of clinician-defined lipodystrophy was associated with a decrease in MI risk.

This important study is one of the first well-designed studies to demonstrate an increased risk of cardiovascular disease among persons treated with HIV therapies. Despite this risk, it remains important to note that the overall life-sustaining benefits of combination HIV treatment vastly outweigh the risks of therapy defined in this study. Measures to reduce other cardiovascular disease risk factors such as smoking and treatment of dyslipidemia in antiretroviral treated patients can tilt the balance even further in favor of HIV therapy.

EPIDEMIOLOGY

New data from the CDC presented in Boston⁷ indicate that the number of AIDS cases nationwide has increased for the first time in several years. In addition, the number of new HIV infections in 25 reporting states increased by 8% from 1999 to 2001. The greatest increases in new HIV diagnoses were seen in both men who have

sex with men and heterosexuals. These are disturbing data and suggest that HIV prevention measures are falling far short of the mark.

Further exacerbating the spread of the epidemic is the failure to identify a significant proportion of persons with living with HIV infection. It is estimated that as many as a quarter of all HIV-infected persons in the U.S. do not know that they are HIV positive. Enhanced HIV testing in clinics and correctional facilities can allow for the diagnosis, counseling and treatment of persons who are infected. In addition, interventions aimed at transmission risk reduction can be most effective when applied to those who are aware of their HIV serostatus. Appropriate diagnosis and treatment of infected individuals can reduce viral burden in the blood and genital secretions, likely reducing transmissibility.

CONCLUSION

At a time where every several weeks it seems there is another "major" HIV-related conference, when there are dedicated meetings for everything from antiretroviral resistance to metabolic complications to treatment adherence, the 10th CROI proved to be impressively comprehensive. There were few data specific to the confluence of HIV and corrections, but information regarding strategies to optimize treatment success and reduce drug toxicity, and trends in the epidemiology of the epidemic will serve physicians who treat HIV-infected patients in jails and prisons well. While no major breakthroughs were reported and the news was not always good, the data presented clearly inched our understanding of HIV and its management forward - and, of course, there is always next year.

*Disclosures: Speaker's Bureau:

GlaxoSmithKline, Gilead, Merck, Roche, and Abbott. Grant support from Roche.

FOOTNOTES:

1. Results of the 2NN Study: A Randomized Comparative Trial of First-line Antiretroviral Therapy with Regimens Containing Either Nevirapine Alone, Efavirenz Alone or Both Drugs Combined, Together with Stavudine and Lamivudine. F van Leth, E Hassink, P Phanuphak, S Miller, B Gazzard, P Cahn, R Wood, K Squires, C Katlama, B Santos, P Robinson, R van Leeuwen, F Wit, J Lange, for the 2NN Study Group. Oral Abstract 176. 10th CROI, February 10-14, 2003.
2. Efficacy and Safety of Tenofovir DF (TDF) Versus Stavudine (d4t) When Used in Combination with Lamivudine and Efavirenz in Antiretroviral Naïve Patients: 96-week Preliminary Interim Results. S Staszewski, J E Gallant, A L Pozniak, J M A H Suleiman, E DeJesus, B Lu, J Sayre, A Cheng. Poster 564b. 10th CROI, February 10-14, 2003.
3. Pegylated Interferon Alfa-2b: A New Therapeutic Option in the Treatment of Early-stage HIV Infection. I Schugt, A Kreuter, R

- Schlottmann, A Bader, P Altmeyer, N H Brockmeyer. Oral Abstract 59. 10th CROI, February 10-14, 2003.
4. Didanosine and Tenofovir DF Drug-Drug Interaction: Assessment of Didanosine Dose Reduction. B P Kearney, E Isaacson, J Sayre, H Namini, A Cheng. Poster 533. 10th CROI, February 10-14, 2003.
5. A Two-way Drug Interaction Between Lopinavir/Ritonavir and Phenytoin. M L Lim, S S Min, J J Eron, R Bertz, M Robinson, A Gaedigk, A D M Kashuba. Poster 535. 10th CROI, February 10-14, 2003.
6. Exposure to HAART Is Associated with an Increased Risk of Myocardial Infarction: The D:A:D Study. N Friis-Moller, R Weber, A D'Arminio Monforte, W El-Sadr, P Reiss, F Dabis, L Morfeldt, S De Wit, C Pradier, G Calvo, M Law, O Kirk, C Sabin, J D Lundgren. Oral Abstract 130. 10th CROI, February 10-14, 2003.
7. Preventing New HIV Infections in the U.S.: What Can We Hope to Achieve? R Valdiserri. Plenary Lecture 4. 10th CROI, February 10-14, 2003.

CROI: NEW ANTIRETROVIRAL AGENTS

By Peter Piliero, M.D.*, Associate Professor of Medicine, Consultant, NYS Department of Corrections, Albany Medical College, and David Alain Wohl, M.D.**, The University of North Carolina

In addition to providing data on new antiretroviral agents in existing classes, the 10th Conference on Retroviruses and Opportunistic Infections (CROI) also featured information on novel therapeutic agents. All but one approved drugs for treating HIV currently target one of two viral enzymes (reverse transcriptase and protease); data was presented on new classes of agents that target other viral processes as well.

New Therapeutic Classes

The first new class to arrive since 1996 is the fusion inhibitor class. Data presented on enfuvirtide (Fuzeon), formerly known as T-20, showed that the drug is well tolerated with the main exception being injection site reactions due to a local reaction to the drug. However, it was also shown that like the other classes of antiretrovirals (ARVs), resistance to enfuvirtide can develop, so it should be used with other active ARV agents. Fuzeon was granted FDA approval on March 13; see Inside News (page 7).

Data on the second-generation fusion inhibitor, T-1249, were also presented. When given to 25 patients who failed enfuvirtide, they experienced a significant reduction in viral load. This suggests that T-1249 could be used to rescue enfuvirtide-resistant strains of HIV. Phase 2 studies will begin later this year. Enfuvirtide is expected to be approved by the FDA within the month.

Another novel class of agents known as CCR5 antagonists was presented. CCR5 antagonists block the binding of HIV to the CCR5 receptor on the surface of the T lymphocyte, thereby blocking entry of HIV. In vitro data on three compounds - AK602, TAK-220, and UK-427,857 - were presented. Unlike fusion inhibitors that are given as a subcutaneous injection, these agents will be given orally. All appeared to be potent inhibitors of CCR5 and should be entering Phase 1 trials this year.

Finally, data on approximately 24 HIV-positive patients given a single IV infusion of TNX-355 were presented. This agent is an anti-CD4 antibody that works by blocking the interaction of HIV with the CD4 receptor on T cells by coating the receptor. Significant viral load reductions were seen as far as 21 days after a single infusion. This promising data support further studies using multiple doses.

Existing Therapy Classes

In the existing class category, we heard about a new Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) and two new PI (Protease Inhibitor) candidates that have the potential to overcome preexisting resistance. The data on the GlaxoSmithKline NNRTI and the Roche PI were from *in vitro* studies, but the Tibotec TMC-114 PI given to 50 patients with multi-PI-resistant HIV produced a significant decline in viral load in the first two weeks of therapy.

There were data presented on atazanavir, which is expected to be approved by the FDA this year. This once-a-day PI has been found to be kinder and gentler to lipids than its classmates. In a continuation of a previously-reported study comparing two doses of atazanavir combined with stavudine (d4T) + lamivudine (3TC) versus a combination of the same nucleosides and nelfinavir (NFV), subjects on NFV were switched to atazanavir while those originally assigned to atazanavir continued on this agent. To participate in this study continuation phase, subjects had to have a viral load less than 10,000 copies/mL after 48 weeks on their originally assigned regimen. Overall, the rates of maximal viral suppression were not as impressive as in some recent studies. Approximately 40% to 50% of subjects initially randomized to atazanavir had viral loads below 50 copies/mL after a year of treatment - no different

from NFV. However, among those with low viral loads entering the study rollover, switching from NFV to atazanavir resulted a year later in improved suppression of viral load below 50 copies (a small jump from 44% to 49%) and increased CD4+ cell counts by about 35 cells/mm³. Importantly, LDL cholesterol, HDL cholesterol and triglycerides all improved significantly after the switch.

A catch for this convenient, lipid-friendly PI is its own brand of toxicity. Hyperbilirubinemia somewhat greater than that seen with indinavir (IDV) is very common in persons taking this drug and frank jaundice can be expected in 10% to 20% of patients. The elevated bilirubin is unconjugated (due to inhibition of bilirubin glucuronidation) and importantly does not

reflect chemical hepatitis.

Data regarding the development of resistance to atazanavir suggest this agent will serve best as a first PI rather than as a salvage agent because prior PI experience and resistance is associated with cross-resistance to atazanavir. Development of atazanavir resistance in the ARV-naïve patient with its characteristic I50L mutation actually increases susceptibility to a number of other PIs, which should appear to retain susceptibility to the other available PIs. The combination of this data suggests that atazanavir will be best used as part of an initial PI-containing regimen. It is also likely that in patients receiving PIs who have dyslipidemias and risk factors for cardiovascular disease but limited evidence of PI resistance, substitution with atazanavir will become a popular alternative to lipid-lowering therapy.

*New drugs...
kinder and
gentler PI
therapy...
and new classes
of ARVs.*

Disclosures:

* *Speaker's Bureau: BMS, GSK, Merck, Roche, Gilead.*

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***Speaker's Bureau: GlaxoSmithKline, Gilead, Merck, Roche, and Abbott. Grant support from Roche.*

CROI: CORRECTIONAL UPDATES

By HEPP Report Staff*

Despite the large impact HIV/AIDS is having on correctional populations - and the increasing attention this issue is receiving - only one oral session and one poster at the conference addressed HIV/AIDS among inmates.

Unsafe sex common among recently-released HIV-positive inmates

David Alain Wohl, M.D., of the University of North Carolina, presented results of a study¹ of the post-release sexual practices of 86 HIV-infected state prison inmates. Wohl conducted the study to better understand the extent to which HIV-infected prison releasees contribute to the spread of HIV in communities to which they return.

"We noticed that there are many communities within the US in which the HIV infection rates and the incarceration rates are high," Wohl told conference participants. "And we were wondering if this is more than just a coincidence."

The study found that more than half of the HIV-infected inmates (51%) reported that they had sex soon after they are released from prison (the mean time was six days), and about one third of these individuals (26%) reported that they had unprotected sex with their main sex partner, on average within nine days of being released.

Interviews were conducted during incarceration and within three months after release.

Average prison stays were about one or two years.

More than half (58%) of the study participants were women, 87% were non-white, and 81% were heterosexual. The study was done in North Carolina, a state that does not perform mandatory HIV testing upon entry or exit from prison.

The data were "surprising," Wohl said. Seventy-five percent said they had a "main" sex partner and 78% of these individuals reported having unprotected sex with that person one year before they went to prison. Of the 57% who reported having other sex partners, the average number of partners was eight. The majority of partners in both categories were not known to have HIV infection.

All of the study participants said they had told their main sex partners that they were HIV-positive, but only two-thirds had told their other sex partners.

Thirty percent reported they believed it was "very likely" or "somewhat likely" that they would infect their main sex partner.

"In many communities, prisons facilitate the transmission of HIV by disrupting the social fabric and sexual network...and also by taking people out of the community, locking them up, and then releasing them to the community," Wohl said. "Our experience has been that when people get out of prison,

there are two things they want to do, and one of them is to get a 'Big Mac.'"

Inmate Health Beliefs and Adherence

A poster presentation² by Stephenson, et al examined health beliefs and adherence in a group of 65 North Carolina state inmates with HIV infection. Inmates almost uniformly believed that the PIs are worth taking and likely would prolong their life. Three-quarters trusted that their health care provider prescribed the best HIV medications and offered high-quality medical care. Finally, 68% preferred to self medicate ("Keep On Person") rather than receive Directly Observed Therapy (DOT) due to inconvenience and stigmatization issues.

*DISCLOSURES: Nothing to disclose.

FOOTNOTES:

1. *HIV Transmission Risk Behaviors Among HIV-Infected Individuals Released from Prison.* D A Wohl, L Shain, M Adamian, B L Stephenson, R Strauss, C Golin, A Kaplan. Oral Abstract 36. 10th CROI, February 10-14, 2003.

2. *HIV-related Health Beliefs, Attitudes, and Adherence of Inmates in a Directly Observed Treatment Setting.* B L Stephenson, D Wohl, R D Hays, C E Golin, H Liu, G Simpson, A H Kaplan, N Kiziah. Poster 917. 10th CROI, February 10-14, 2003.

RESOURCES & WEBSITES

10th CROI Webcasts and Abstracts

<http://www.retroconference.org/2003/>

10 CROI Conference Reports

<http://www.natap.org/>

<http://www.thebody.com/confs/retro2003/retro2003.html>

<http://www.medscape.com/viewprogram/2221>

Clinical Guide on Palliative Care of HIV/AIDS Patients

New HHS guidelines for clinicians on providing palliative and supportive services to patients living with HIV/AIDS. Copies of the guide are available online at <http://hab.hrsa.gov> or may be ordered from the HRSA Information Center at 1-888-275-4772.

Gender and HIV/AIDS Web Portal

A new online resource addressing gender-specific knowledge and information. Sponsored by the United Nations Development Fund for Women, the site offers research, training materials, surveys, advocacy tools, current news and opinion pieces by leading experts, and women's stories from the field.

<http://www.GenderandAIDS.org>

The Body Pro: The HIV/AIDS Resource for Healthcare Professionals

A new online resource for HIV/AIDS health care professionals. News, treatment strategies, conference coverage, and "treatment library." Free one-time registration required for some content and services. <http://www.thebodypro.com>

Nursing Care of the HIV-Infected Inmate: A Monograph Series Continuing nursing education credit available. Module 1, available now: "HIV Pathogenesis." Module 2, available in March: "HIV Medication Overview." From the Albany Medical Center and sponsored by Gilead Sciences, Inc.

http://www.amc.edu/Patient/hiv/hiv_modules.htm

HIV Correctional Health Care Resources

Correctional health care resources including videoconference series, videotapes, and correctional education abstracts.

http://www.amc.edu/Patient/hiv/hiv_correctional.htm

PDA-Formatted Guidelines Available

The U.S. Department of Health and Human Services has posted guidelines that can be downloaded and viewed in Palm OS or Pocket PC PDAs. Guidelines include Health Care Worker Exposure, Tuberculosis, Opportunistic Infections, Adult & Adolescent Antiretroviral Therapy, Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy, and Hydroxyurea.

<http://aidsinfo.nih.gov/mobile/>

CDC Public Health Emergency and Preparedness Response

Info, training, and resources for preparing and responding to bioterrorism, including smallpox and anthrax.

<http://www.bt.cdc.gov/training/index.asp>

SAVE THE DATES

Improving the Management of HIV Disease

March 28, 2003
New York, New York
Email: cme@iasusa.org
Visit: www.iasusa.org/cme/

15th National HIV/AIDS Update Conference

Focusing on the Front Lines: Practical Lessons in Prevention, Treatment, and Care
March 30-April 2, 2003
Miami, Florida
Email: nauc@total.net
Visit: www.amfar.org/nauc

2003 ACHSA Multidisciplinary Training Conference

Health Services and Security Working Together in Harmony
Co-hosted by the CDC and HRSA
April 10-13, 2003
Baltimore, Maryland
Call: 877-918-1842
Email: achsa@mindspring.com
Visit: www.corrections.com/achsa

Clinical Updates in Correctional Health Care NCCHC Spring Meeting

April 12-15, 2003
Anaheim, CA
Call: 773.880.1460
Visit: www.ncchc.org

9th Annual Jail Health Conference

May 12-13, 2003
Wisconsin Dells, Wisconsin
Visit: <http://www.uwec.edu/CE/>

43rd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)

September 14-17, 2003
Chicago, Illinois
Call: 202-737-3600
Email: icaac@asmusa.org
Visit: www.icaac.org/ICAAC.asp

The United States Conference on AIDS

Sponsored by the National Minority AIDS Council
September 18-21, 2003
New Orleans, Louisiana
Call: 202-483-6622
Visit: www.nmac.org

National Conference on Correctional Health Care

October 4-8, 2003
Austin, Texas
Call: 773-880-1460
Visit: www.ncchc.org

INSIDE NEWS

FDA Approves Fuzeon

The Food and Drug Administration (FDA) granted accelerated approval of enfuvirtide (Fuzeon) for use in combination with other anti-HIV medications to treat advanced HIV infection. Fuzeon, also known as T-20, is the first product in a new class of medications called fusion inhibitors to receive marketing approval. Unlike existing drugs that work inside the cell, Fuzeon blocks HIV from entering healthy immune cells. The drug was designed for patients in advanced stages of the disease who have shown resistance to other AIDS drugs, and is indicated for the treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy. Fuzeon is administered twice-daily as a subcutaneous injection. Local injection site reactions were the most common side effects reported, and approved labeling warns physicians to carefully monitor patients for signs and symptoms of pneumonia.

Developed with Trimeris Inc. and Roche Pharmaceuticals, Fuzeon will be distributed by Roche. Initial demand for Fuzeon is expected to outstrip supply, and the companies are still working on a distribution plan. The U.S. price has not yet been finalized, but is expected to reach new records for drug pricing based on the price set in Europe at 52 euros a day, or more than \$20,000/year. Roche says the high cost (more than double the cost of other HIV/AIDS drugs on the market) is due to the complexity of the manufacturing process, which involves more than 100 production steps. *FDA News and Reuters, 3/14/03*

Trizivir Trial Halted: Less Effective When Taken Alone

The National Institutes of Health (NIH) halted a trial of GlaxoSmithKline's Trizivir (abacavir sulfate/lamivudine/zidovudine) after it proved less effective than when used in combination with other AIDS drugs. The study involved 1,147 treatment-naïve patients and compared Trizivir alone with a combination of Trizivir and Sustiva (efavirenz), and a combination of Sustiva and Combivir (lamivudine/zidovudine). The NIH decided to stop the Trizivir-only arm of the trial after participants in that arm experienced virologic failure sooner and more often than patients in the other two arms of the study. After an average of 32 weeks in the study, 167 participants out of 1,147 experienced virologic failure; 21% of the patients taking Trizivir alone experienced failure, compared with 10% in the other two arms of the study. The trial comparing the other combinations will continue. *Wall Street Journal and Reuters, 3/13/03*

FDA Issues Alert About Counterfeit Procrit

The US Food and Drug Administration warned about counterfeit versions of Procrit (erythropoietin) that are ineffective and contaminated with bacteria that could harm patients. Laboratory testing discovered the three lots of the counterfeit Procrit with the following lot numbers and expiration dates: P007645, expiration 10-2004;

P004677, expiration 02-2004; and P004839, expiration 02-2004. If a counterfeit version is found, it should be quarantined and the FDA should be notified (1-800-835-4709). *FDA News, 3/11/03*

NEJM: Antiretroviral Drugs Have Lower Heart Attack, Stroke Risk Than Previously Stated

Contrary to data presented at the 10th CROI (see the results from the D: A: D study discussed in the main article), antiretroviral drugs do not cause "premature" heart attack or stroke in HIV-positive patients, according to a study published in the Feb. 20 issue of the *New England Journal of Medicine*. Samuel Bozzette et al. conducted a retrospective study of almost 37,000 patients who received care for HIV infection at Veterans Affairs facilities nationwide between 1993 and 2001. "Use of newer therapies for HIV was associated with a large benefit in terms of mortality that was not diminished by any increase in the rate of cardiovascular or cerebrovascular events or related mortality," the authors state. *New England Journal of Medicine, 2/20/03*

Boehringer Ingelheim Launches Phase III Clinical Trials for Tipranavir

Boehringer Ingelheim (BI) launched Phase III RESIST clinical trials to study the efficacy and safety of tipranavir for use in combination therapy for HIV infection. Tipranavir is the first non-peptidic protease inhibitor (NPPI) in development for the treatment of HIV infection. The RESIST trials will evaluate triple-class-experienced patients in more than 280 clinical trial sites worldwide. *PRNewswire, 2/6/03*

Officials Urge Increased Use of HIV Rapid Test

CDC officials at the 10th Conference on Retroviruses and Opportunistic Infections (CROI) called for more widespread use of a rapid HIV test approved by the FDA in November 2002. More widespread use could help curb the spread of the disease by identifying newly-infected people as soon as possible in order to reduce their chance of transmitting the virus to others. The rapid test also can be very useful in the setting of post-exposure management of health care workers when the source's HIV status is not known. Officials recommended that the new test, which can provide results in 20 minutes, be part of routine health care for those at risk of infection.

Boston Globe, 2/11/03

Nearly 41% of South Africa's Prison Population is HIV-Positive

A study released by the nongovernmental Institute for Security Studies estimates that nearly 41% of inmates in South Africa's "overburdened" prisons are infected with HIV/AIDS. Since 1995, reported cases of HIV/AIDS in South African prisons rose by 750%, and the number of natural deaths in prison have surged by about 600 percent. Most of the deaths are believed to be AIDS-related. According to Reuters, the disease's progress is being hastened by severe overcrowding in the prisons. *Reuters, 2/18/03*

SELF-ASSESSMENT TEST FOR CONTINUING MEDICAL EDUCATION CREDIT

Brown Medical School 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 September 30, 2003. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. A recent study of HIV+ inmates' sexual behavior after release from prison found that:
 - (a) 70% had sex with their main sex partner within nine days of being released from prison.
 - (b) 45% had other sex partners in addition to their main sex partner.
 - (c) 26% had unprotected sex with their main sex partner after being released.
 - (d) None of the above

2. The same study of HIV+ inmates' sexual behavior after release also found that:
 - (a) All of the study participants reported that they informed their main sex partner of their HIV+ status.
 - (b) Only two-thirds of the study participants stated that they told their other sex partners of their HIV+ status.
 - (c) Thirty percent reported they believed it was "very likely" or "somewhat likely" that they would infect their main sex partner.
 - (d) All of the above.

3. Data presented about atazanavir during the 10th CROI show that the agent is commonly associated with the following side effects:
 - (a) Injection site-reaction
 - (b) Hyperbilirubinemia
 - (c) Elevated serum creatinine levels
 - (d) Increased triglycerides

4. Results from the 903 Study, which compared the efficacy and safety of a treatment regimen of tenofovir, lamivudine and efavirenz to a regimen of stavudine, lamivudine and efavirenz showed that:
 - (a) The stavudine arm was much more effective in decreasing HIV viral load than the tenofovir arm.
 - (b) The tenofovir arm was much more effective in decreasing HIV viral load than the stavudine arm.
 - (c) The stavudine and tenofovir arms were equally effective in decreasing HIV viral load, and patients on the stavudine arm experienced substantially less lipodystrophy and lower elevations in fasting cholesterol and triglyceride levels.
 - (d) The stavudine and tenofovir arms were equally effective in decreasing HIV viral load, and patients on the tenofovir arm experienced substantially less lipodystrophy and lower elevations in fasting cholesterol and triglyceride levels.

5. At the 10th CROI, the CDCP reported that the greatest increases in new HIV infections are now occurring in:
 - (a) Injection drug users
 - (b) Men who have sex with men
 - (c) Heterosexuals
 - (d) Both men who have sex with men and heterosexuals

6. Data presented at the 10th CROI demonstrated that:
 - (a) Tenofovir increases the serum levels of ddl.
 - (b) ddl increases the serum levels of tenofovir.
 - (c) Lopinavir-ritonavir increases the serum levels of phenytoin.
 - (d) Tenofovir increases the serum levels of efavirenz.

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