



HEPP NEWS

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HIV EDUCATION PRISON PROJECT

Sponsored by the Brown Medical School 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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SEXUALLY TRANSMITTED DISEASE IN PEOPLE INFECTED WITH HIV

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Sexually transmitted diseases (STDs) constitute an important source of morbidity in incarcerated patients. In addition, the presence of an STD is a clear sign of HIV risk behavior. The presence of an STD in an inmate should (1) stimulate a discussion of HIV risk behaviors; (2) prompt a discussion of the need for follow-up HIV testing; and (3) provide an opportunity to teach inmates about the facilitating role some STDs play in HIV transmission. This article reviews the diagnosis and treatment of common STDs and highlights differences in the clinical presentation or management of STDs in the HIV infected patient.

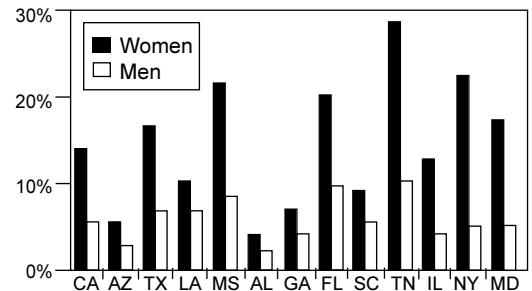
Epidemiology

Numerous studies have documented high rates of incident STDs in people with HIV (1,2). Though STD rates in people with HIV declined in the early years of the HIV epidemic (3,4), recent reports of rising numbers of cases of gonorrhea, chlamydial infection and syphilis mandate a state of vigilance, particularly among inmates who have participated in unsafe sexual practices (5). These rising STD rates are concerning not only because they suggest increased levels of unsafe sexual behavior, but also because gonorrhea, syphilis, HSV, and other STDs are associated with increased HIV shedding in genital secretions and, consequently, increased HIV transmission (6).

STDs in Prisons and Jails

Limited information on the prevalence of STDs among prison and jails inmates is available. One study, however, estimated that approximately 210,000-345,000 (2.6-4.3%) of inmates released from prisons and jails in 1997 had syphilis at the time of release, 184,000 (2.3%) had chlamydia, and 70,000 (1%) had gonorrhea (7). Studies of women in New York City jails found a much higher prevalence of STDs; 35% of jailed women had syphilis at the time of arrest, 27% had chlamydia and 8% had gonorrhea (8, 9). In a separate study, the rate of syphilis infection was determined to be 1000 times higher among women admitted to New York City jails in 1997 (6.5 infections per 100 woman-years) than the rate of syphilis among women in the surrounding community (New York City) (8).

FIGURE 1. Syphilis (RPR+) Prevalence Among Incarcerated Men and Women in Select States (1997)



Adapted from the CDC report: Local and State STD Control Programs; Regional Infertility Prevention Programs.

TREATMENT OF STDs IN HIV-INFECTED PATIENTS Syphilis

Case reports and case series early in the course of the AIDS epidemic suggested that patients with HIV may be prone to more rapid progression of syphilitic disease and atypical clinical presentations. (See figure 1) In particular, patients with HIV were reported to have early ocular or neurological involvement, gummatous lesions, ulcerative skin lesions and persistent chancres. More recently, a large prospective study of 101 HIV-infected and 440 HIV-uninfected patients with syphilis found that patients with HIV were more likely to have multiple chancres and a slow serologic response to therapy, but were not more likely to have early ophthalmic or neurosyphilis (10).

The laboratory evaluation of syphilis can be altered by HIV. Typically, this evaluation consists of non-treponemal screening tests (RPR) and confirmatory testing with specific treponemal tests (MHA-TP, TPHA, or FTA) when the RPR is positive. Patients with HIV may have atypical results from all of these tests. Among injection drug users with or without HIV, biological false positive results on non-treponemal serological tests (RPR or VDRL) are more com-

Continued on page 2

WHAT'S INSIDE

CTC Update	pg 5
HIV 101	pg 7
Save The Dates	pg 8
Self-Assessment Test	pg 9

STDs... (continued from page 1)

mon (thus a positive RPR or VDRL is always followed by a more specific test). In addition, people with HIV are more likely to revert to a negative treponemal test following treatment (11).

In cases where syphilis infection is present (a positive RPR and confirmatory test such as an FTA), clinicians should carefully evaluate the patient and stage the infection. Which patients require lumbar puncture (LP) for presumed tertiary syphilis is controversial. CDC recommends that LP be performed on HIV- and syphilis-infected patients with neurological or ocular symptoms, those with late latent syphilis (>1 years duration), and those who experience a rise in titer following treatment or fail to have at least a 2-dilution decline in serum titer within 6-12 months following therapy. Clinicians should consider performing treponemal tests on cerebrospinal fluid (CSF) for patients with HIV, as other signs of tertiary syphilis (elevated CSF protein and pleocytosis) may be associated with HIV infection and may obscure results. (12)

Case reports of treatment failure, the delayed serological response to therapy, and the recognition of the role typically played by the cellular immune response in controlling syphilis have raised concerns about the adequacy of standard syphilis treatment regimens in HIV patients. To date, prospective studies have not demonstrated that conventional treatment is associated with an elevated risk of treatment failure and CDC treatment recommendations for syphilis do not differ for patients with HIV (see HIV 101, Page 7)(13). However, even the largest published study was not adequately powered to exclude the possibility that HIV patients are at significantly elevated risk of treatment failure. Consequently, extra vigilance is required in monitoring HIV patient's response to therapy and repeat serological testing should be performed 3, 6, 9, 12 and 24 months after treatment.

Herpes simplex virus (HSV)

Genital herpes simplex virus (HSV) infections are extremely common in incarcerated HIV-infected patients. Typical manifestations of genital herpes include pustules, vesicles, ulcers and crusted genital lesions. However, viral shedding in the absence of symptoms or with only mild symptoms such as genital tingling, itching or numbness is common. HSV can also cause urethritis, cervicitis, atypical appearing perianal ulcers and fissures, and proctitis. Diagnosis is usually made clinically but can be confirmed by direct fluorescent antibody testing or viral culture of specimens taken from lesions using a Dacron swab.

In people with HIV, herpes can cause extremely painful and severe lesions that are slow to respond to therapy. Clinical occurrences of HSV reactivation, both symptomatic and asymptomatic, increase

TABLE 1. Jail Facilities with Policies of Offering STD Testing (1997)

POLICY	CHLAMYDIA		GONORRHEA		SYPHILIS	
	#	%	#	%	#	%
Provide Routine Testing*						
Women	20	20%	23	22%	48	47%
Men	13	12%	17	16%	49	46%
Provide Testing to Arrestees Presenting symptoms or Request Testing*						
Women	74	72%	73	72%	53	52%
Men	46	71%	82	77%	57	53%
Routine Screening Cost Effectiveness/Savings^A						
Women	\$112 per case prevented (cost effective)		\$266 per case prevented (cost effective)		\$62 cost saving per case	

*Data taken from a survey of 115 city and county jails and reported in *Assessment of Sexually Transmitted Diseases Services in City and County Jails-United States, 1997*. MMWR June 5 1998; 47(21):429-431.

^ Data taken from a report presented by Julie Kraut, PhD "The Cost Effectiveness of Routine Screening for Sexually Transmitted Diseases in United States Prisons and Jails" for the National Commission on Correctional Health Care, June 15, 2999.

in frequency and duration at lower CD4 counts. CDC recommendations for the treatment of genital herpes in patients with HIV do not differ from those without HIV. However, because response to therapy can be delayed, treatment should be continued beyond the standard 10 days if ulcers have not healed or if new lesions continue to appear. Chronic suppressive therapy with anti HSV agents such as Acyclovir (or derivatives such as Famcyclovir or Valacyclovir) have been shown to decrease the frequency and duration of symptomatic outbreaks of genital HSV as well as asymptomatic HSV shedding in patients with HIV. Suppressive treatment should be considered in patients with frequent or severe recurrences (14). While acyclovir resistance has very seldom been a problem in immunocompetent patients, resistance does occur in the context of HIV associated immunosuppression and, resistance testing should be performed in HIV-infected patients who fail to respond to therapy. Foscarnet is the drug of choice to treat resistant virus.

Human Papillomavirus (HPV)

More than 100 different human papillomaviruses (HPV) have been detected and, combined, these viruses are the most common STD. Current studies suggest that over 50% of sexually active adults have been infected with one or more HPV types (15). Most often, HPV infection causes genital warts, however some types of HPV infection are linked to cancer. While overlap in clinical manifestations exists, HPV types 16, 18, 31 and 35 are responsible for most cases of cervical and anal cancer, while types 6 and 11 are the most common causes of genital warts.

Anogenital warts most commonly present as verrucous (cauliflower appearing) or papular lesions (condyloma acuminata). Less frequently, warts can be keratotic (like palmar warts), smooth (dome-shaped), or flat. Flat warts are more common within the vagina. Warts can occur anywhere in the anogenital area and usually are asymptomatic, though some patients complain of rectal discomfort, itching, burning or dis-

charge, symptoms that they frequently attribute to hemorrhoids. HIV patients with CD4 counts below 50 are more likely to have diffuse condylomatosis. At higher CD4 counts, extensive warts and the prevalence of HPV of low oncogenic potential do not appear to be increased (16).

Therapy for genital warts can be divided into patient applied-treatments and provider applied or administered treatments (see HIV 101, page 7). An excellent review of these treatments was recently published (17). CDC recommendations for wart treatment do not differ for people with HIV. No consensus exists regarding a single best approach, therefore decisions regarding care need to factor in patient preference, patient ability to follow application instructions, wart location and accessibility, and cost. Referral to a specialist is indicated if no improvement is seen after 3 treatments, complete clearance has not occurred after 6 treatments, or continued treatment would extend beyond the duration recommended by manufactures of patient applied therapy. Over treatment should be avoided. Unfortunately, recurrence of warts following treatment is extremely common. Patients with more extensive initial disease are more prone to recurrence. Treatment with HAART has been associated with a significant decline in wart recurrence (18).

HIV-related immunosuppression is associated with an elevated risk of genital shedding of oncogenic HPV types, cervical and

Continued on page 4

GLOSSARY:

- CDC:** Centers for Disease Control
- CNS:** central nervous system
- CSF:** Cerebrospinal fluid
- FTA:** Fluorescent treponemal antibody
- HAART:** Highly active antiretroviral therapy
- LP:** Lumbar puncture
- MHATP:** Microhemagglutination assay for antibody to *Treponema pallidum*
- STAT RPR:** rapid plasma reagin
- STDs:** sexually transmitted diseases
- VDRL:** Venereal Disease Research Laboratory

LETTER FROM THE EDITOR

Dear Colleagues,

Whenever I see a patient with a sexually transmitted disease in my prison HIV practice, my mind invariably travels back to a prison for women in Framingham, Massachusetts, where an STD nurse by the name of Virginia Cram reigned the intake facility. Ginny never lost an opportunity to teach her "girls" about the link between STDs and HIV infection. Every time she discovered an STD, she pushed her patient to agree to get tested for HIV infection because, as she said, "if you got that infection - just imagine what else could have been sashaying around down there..." She taught the women in her care that STDs are linked to HIV - not only because they are chummy fellow travelers, but also because STD infections can increase the risk of acquisition of HIV. Ginny's style of intervention was extremely effective - many of her girls did get tested for HIV infection, and I like to believe that some of the Framingham women may have avoided HIV infection as a result of her effort to use every STD treatment as an educational opportunity.

The importance of screening for STDs in prison and jail settings and treating those infections cannot be overemphasized. Screening for syphilis has been shown to be a cost-saving public health intervention in jails - and screening for other STDs is extremely cost effective particularly in locations where STD prevalence is high. Rapid tests such as the Stat RPR and rapid chlamydia screening tests have facilitated the treatment of STDs, making their management completely feasible, even in the high turnover setting of a city jail. Implementation of the Stat RPR in the Cook County jail system in Chicago has had a tremendous impact on overall syphilis rates in Chicago, underscoring, once again, the impact of prison and jail interventions on public health.

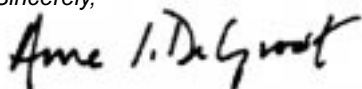
After reviewing this issue of HEPP News, readers should be able to describe the epidemiology and treatment of syphilis, chlamydia, trichomonas, herpes, and warts in an HIV-infected patient.

Next month, Kris Herfkens from North Carolina will discuss mental health issues in treating HIV infected patients, and HEPP News will provide tools for diagnosis of mental health conditions.

We are pleased to announce that as of Friday, December 22, Continuing Medical Education (CME) credit will be available online through HEPP News at www.HIVcorrections.org! Try it out this week!

And finally, we wish you all a happy and safe holiday!

Sincerely,



Anne S. De Groot, M.D.

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STDS...*(continued from page 2)*

anal dysplasia, invasive cervical cancer and possibly anal cancer. Incarcerated women with HIV infection should have regular Pap screening. Many correctional institutions have set guidelines for performing Pap smears every 6 months for incarcerated women as they belong to a very high risk group with limited access to healthcare outside correctional facilities. Care is then based on Pap smear results as detailed in published guidelines (19). While some authorities have advocated anal Pap smears be done on men with HIV, the natural history of anal dysplasia remains ill-defined and the utility of Pap smears in preventing cancer is controversial. Current guidelines do not recommend anal Pap smears for men (20). However, clinicians should have a low threshold for performing biopsies on suspicious lesions.

Gonorrhea and Chlamydial Infection

Neisseria gonorrhoeae and *Chlamydia trachomatis* are common causes of STD in people with HIV. Gonococcal urethritis is symptomatic in over 80% of cases, however, chlamydial urethritis is asymptomatic in as many as 50% of cases, and most cervical, pelvic and anorectal infections with both pathogens are asymptomatic. Urethral Gram stain is 95% sensitive in detecting gonorrhea, but rectal and cervical testing are much less sensitive, and culture or DNA amplification testing are generally required to make a diagnosis. Laboratory tests for detecting *Chlamydia trachomatis* vary in sensitivity from 30-98% (21). DNA amplification testing is most sensitive and is recommended when available. HIV is not known to affect the natural history of these infections in men, however, pelvic inflammatory disease in women with HIV may be more protracted and the risk of tubo-ovarian abscess may be increased (22). Recommended treatment of these infections is the same as for non-HIV infected persons.

Vaginal discharge: *Trichomonas*, *Candida*, and "Bacterial Vaginosis"

Trichomonas vaginalis, a protozoan STD, is a common cause of vaginal discharge, may increase the risk of transmission of HIV, and may also predispose pregnant HIV-infected women to premature rupture of membranes and early labor. Diagnosis is difficult, since the symptoms of trichomoniasis mimic those of other STDs and detection methods lack precision. Although current treatment protocols involving nitroimidazoles are curative, reinfection is common among incarcerated women. Yeast (*Candida albicans*) infections are also extremely common among HIV-infected women and recurrent vaginal yeast infections may be the first presentation of HIV infection. Topical treatment is usually effective, however chronic suppression with oral fluconazole is necessary in some cases of frequent recurrence. Resistance may occur. Bacterial vaginosis, the most common cause of vaginal discharge or malodor, is caused by mixed flora including anaerobic

bacteria, *Gardereella vaginalis*, and *Mycoplasma hominis*. Metronidazole is effective.

STD SCREENING IN INCARCERATED POPULATIONS OF PEOPLE WITH HIV

A major challenge for STD treatment is related to the high population turnover rate - more than 50% of arrestees are released within a 48 hour period (8, 22). This high turnover rate makes STD screening an even more important public health intervention. However, despite widespread knowledge about the high STD prevalence among newly incarcerated women and men, less than half of city and county jails surveyed in a CDC study had implemented "routine STD screening" policies. Most facilities polled for the study said that STD testing was performed only if a patient requested the test or if the patient presented with STD symptoms (see Table 1) (23).

In light of these challenges, correctional facilities should develop routine STD screening programs, especially for persons with HIV (24). STD screening should be performed fairly regularly after incarceration (in conjunction with Pap smears) as both HSV and *Trichomonas* have been noted to be increased in HIV-infected incarcerated women.

Chlamydia and Gonorrhea

The CDC recommends chlamydial screening for all sexually active women under age 20, women 20-24 with either more than one partner in the preceding 60 days or a history of inconsistent use of barrier contraception, and women 25 and over with both of these risk factors. Many recently incarcerated women would qualify for gonorrhea, syphilis, and chlamydia screening by these criteria.

Over the last decade, chlamydial screening programs have been established in some correctional facilities in the U.S, though most US city and county jails test for STDs only if inmates present for symptoms (25). The prevalence of chlamydia infection detected by jail based screening programs has generally vastly exceeded that seen in non-incarcerated populations (26).

Human Papillomavirus (HPV)

HPV-associated cervical cancer can be prevented by routine Pap screening. Among HIV-infected incarcerated women, 6-monthly or annual pelvic exams for Pap smears are already part of routine HIV care.

Syphilis

Screening for syphilis in jail populations has been shown to be cost-saving, however, screening is still not routine in many facilities (Table 1) (23). Screening should be routine for all incarcerated HIV-infected patients at the time they initiate care for HIV (if not already performed at intake). The RPR test should be repeated annually, regardless of whether or not patients are released to the community and return to prison (27). Clinicians should maintain a low threshold for

See HIV 101 on page 7 for STD Treatment Guidelines.

repeating the RPR test in the assessment of patients with genital ulcers, new rashes of uncertain etiology and changes in mental status.

A study at the Cook County Jail in Chicago (CCJ) demonstrates the public health importance of syphilis screening in corrections. CCJ used the "stat RPR" test to screen for syphilis. As a result, the number of cases identified at the CCJ increased from 10% of Chicago's total to 22%. After implementation of the Stat RPR protocol in the CCJ, cases of early syphilis rates for women in the Chicago actually decreased by 24%. This certainly suggests that declining syphilis morbidity in the city might be related to increased screening and improved treatment (24).

Another approach, implemented in NYC, involved developing an algorithm for triaging patients based on RPR tests and city records. Use of this algorithm led to an increase in the number of patients treated for syphilis from 7% to 84% of women and 88% of pregnant women. Seven out of eight babies who might otherwise have required treatment for congenital syphilis did not need to be treated because their mothers were adequately treated while incarcerated (8).

Screening for STDs in men

Very little data on screening for STDs in HIV infected incarcerated men currently exists. Given the important role that asymptomatic, prevalent STDs may play in HIV transmission, it seems reasonable to err on the side of extra screening as data accumulates. One approach is to screen at least annually for rectal gonorrhea and chlamydial infection by culturing all men who may have engaged in receptive anal intercourse, screen all recently incarcerated men for urethral chlamydial infection, and culture the pharynx for gonorrhea in patients who may have engaged in receptive oral sex (28).

CONCLUSION: COUNSELING IS KEY FOR PREVENTION

Counseling about safer sexual habits should be a routine part of the screening process. Providers should emphasize that adopting safer behaviors is important not only to prevent HIV transmission, but also to safeguard the patient's individual health. It is important to use every STD clinic visit as an opportunity to educate the patients about well recognized and common STDs (gonorrhea, chlamydial infection, syphilis, herpes, warts) as well as diseases that many patients may not generally associate with sexual transmission, such as cervical and anal cancer, Kaposi's sarcoma, and, possibly, drug-resistant HIV. In cases of bacterial STDs and HIV, providers should emphasize the importance of notifying sex partners and, when needed and possible, should request the assistance of public health authorities to do so.

STDs...(continued from page 4)

*Nothing to disclose.

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A YEAR OF INVESTIGATION: UPDATE ON CLINICAL TRIALS IN CORRECTIONAL SETTINGS

by HEPP News Staff

Research involving prison inmates saw an uncharacteristic amount of attention from the Department of Health and Human Services immediately following HEPP News' October 1999 conference on clinical trials in correctional settings. Between November 1999 and June 2000, the Office for Human Research Protection (OHRP) (then the Office for Protection from Research Risk, OPRR) investigated the institutional review boards (IRBs) for prison research projects in four states, Rhode Island, Connecticut, Florida, and Texas. The OHRP acts under the secretary of the HHS in order to review all human subject research (See OHRP Regulations on the internet at <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>). After investigations and responses by the IRBs responsible for each of the research projects, most of the research has resumed.

Rhode Island: Miriam Hospital and Brown University

After conducting an internal audit of the IRB review procedures for prison protocols, the Miriam Hospital (TMH) in Rhode Island reported their findings to the OHRP in December of 1999 (1). According to the manager of the Lifespan Research Review Committee, the IRB was unclear on the HHS regulations regarding review of research involving prisoners (see Table 1, below). As a result of the audit report, the OHRP provided TMH with clarified guidelines and suspended TMH projects involving prisoners until TMH re-reviewed the prison protocols using the clarified guidelines (2) and submitted new protocols to be approved by the OHRP. The OHRP subsequently approved TMH's research protocols and the projects have been resumed.

The OHRP also contacted Brown University directly with questions regarding research projects involving prisoners. According to Thomas Wunderlich, Associate Dean for Research at Brown, the university provided a detailed response. Recently, after reviewing Brown's response, OHRP notified Brown of its determinations requiring the University to take specific actions as well as provide additional information to OHRP addressing issues and concerns related to Brown's procedures for protecting prisoners as human subjects in research.

Connecticut: Yale University and CT DOC

OHRP also audited Yale University's prison research (no clinical trials were being conducted, however several observational studies were taking place). OHRP concerns included the following: in several of the IRB meetings, no prisoner representative was listed as participating, Yale IRB failed to conduct annual review for two research projects, and they were cited for having insufficient "policies and procedures that adequately describe their activities according to HHS regulations." (3) Jackee Weaver in the Yale Public Affairs office stated that Yale had prepared a formal response that had probably already been sent to the OHRP, and that this letter was not public information.

Florida: U. Miami and Florida DOC

The OHRP was also concerned with Florida's prisoner representation on the University of Miami's (UM) IRB for protocols involving Florida prison inmates. OHRP found that the prisoner representative on the UM IRB did not have voting privileges, and may have had conflicting interests because he was also an employee of the Florida Department of Corrections (4).

According to Dr. David Thomas, Medical Director for the Florida Department of Corrections, UM and FDOC responded immediately to the OHRP's concerns. Dr. Thomas commented, "Although the OPHR found some discussion [in prison research protocols] of payment for clinical trials, at no point in time were Florida Department of Corrections prisoners . . . offered any form of compensation for [participation in] clinical trials. At the outset of the program this was discussed and [it was] decided that for the inmates and the system this may smack of coercion and [therefore the proposal] was rejected." Ultimately, none of the studies involving FDOC inmates were found to be in violation of HHS regulations, therefore all of the studies were allowed to continue.

Texas: UTMB and the Texas DOC

In Texas, approximately 250 protocols involving prisoners were reviewed by the OHRP. HIV research was the subject of only a few of the protocols. In July, OHRP suspended

Continued on page 6

A YEAR OF UPDATES...

(continued from page 5)

220 protocols. Investigators conducting 26 research protocols were allowed to continue currently enrolled prisoner subjects in "the interest of their health or well-being." (5) The OHRP requested that UTMB provide a detailed list of suspended protocols and re-review a number of protocols under the full IRB. Lastly, the prisoner research protocol suspension was required to remain in place until UTMB had a new prisoner advocate (according to UTMB, the new representative was recently accepted by OHRP), and until UTMB re-reviewed those protocols requesting inclusion of prisoners.

Glaxo Wellcome's HIV studies in Prisons

Glaxo Wellcome had at least two studies involving prisoners as human subjects when the OHRP began their investigation of prison research this year. NZTA4006, 4007 studied genotypic patterns after virologic failure. The second study reviewed adherence among inmates on compact triple nucleoside therapy. Glaxo research sites included correctional facilities in Florida, Rhode Island, Texas, South Carolina, and Arkansas, under a central IRB. According to company spokespersons, no problems were found in Florida, Rhode Island, South Carolina, or Arkansas. In Texas, new enrollment in those studies was suspended. Some of the subjects in NZTA4007 were "rolled over" into another protocol (ESS4005) which includes patients inside and outside the correctional system (6).

Results from the studies performed in Texas, Florida, and Rhode Island were presented at the 5th International Congress on Drug Therapy in HIV Infection (Glasgow, UK 22-26 October 2000) (7,8), and a manuscript is in preparation. Some of the subjects in NZTA4007 were "rolled over" into another protocol (ESS4005) which includes patients inside and outside the correctional system.

For-profit companies can obtain IRB approval for studies involving human subjects from for-profit (and not-for profit) IRBs. These

boards are required to review the studies according to FDA regulations (see FDA regulations in Table 1). If, however, the institution has "multiple project assurance" (MPA) with HHS and has indicated that it will review all research in accordance with that assurance, regardless of whether the research is supported or conducted by the Department, then the IRB is bound to review and approve or reject protocols in accordance with OHRP regulations.

Expanding the Review Process

The new HHS investigative branch, OHRP, found that Rhode Island, Texas, Florida and Connecticut responded appropriately to the OHRP investigations. The need for research involving prison inmates, however, continues to grow, adding to what HHS secretary Donna Shalala recognizes is an already overwhelmed IRB system. In a letter to the *New England Journal of Medicine*, Shalala underscores the need for IRBs and research institutions to adhere to existing HHS regulations and strengthen current IRB review processes (*NEJM*, September 14, 2000; 343(11): 808-810, also available at <http://www.nejm.org/content/2000/0343/0011/0808.asp>). Shalala writes, "Aggressive recruiting by researchers who have been offered money or other inducements [for recruiting subjects] may be contributing to the erosion of informed consent." The new OHRP intends to clear up possible violations of HHS regulations and ensure that IRBs closely follow these guidelines. According to Shalala, "Much brilliant biomedical research is being done in universities and academic health centers... and we [the federal government] have a responsibility to make sure the money we invest...is not used in ways that harm people participating [in that research]." (9)

The complete reports from the Conference on Clinical Trials in Corrections in Providence, Rhode Island October 13-15, 1999 have been published in the Journal of Medicine and Health, Rhode Island. For copies contact the Rhode Island Medical Society at 401.331.3207.

References:

1. Letter, August 28, 2000, from Sanford Leikin, MD, Compliance Oversight coordinator, Division of Human Subjects Protections, to Peggy McGill, Office of Research Administration-Lifespan, The Miriam Hospital, Providence, Rhode Island.
2. These guidelines are available at <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/prison.htm>.
3. Letter, July 27, 2000 from Carol J. Weil, JD, Compliance Oversight Director, Division of Human Subject Protection, Health and Human Services to Dr. Alison F Richard, Provost, Yale University.
4. Letter, July 31, 2000 from Sanford Leikin, MD, Compliance Oversight coordinator, Division of Human Subjects Protections, to Norman Altman, University of Miami, FL; Ira Clark, Public Health Trust, Miami FL; and Gus Godoy, VA Medical Center, Miami FL.
5. Letter, July 10, 2000, from Michael A. Carome, Chief, Compliance Oversight Branch, Division of Human Subject Protections, OHRP to Dr. Dorothea Wilson, Vice President for Research, UTMB.

6. Kirkland, L, Fischl, M, Tashima, K, Paar, D, Gensler, T, Graham, N, Gao H, Hessesenthaler, S, Hernandez, J. Abacavir and Combivir given under Directly Observed Therapy is a potent HAART Regimen - Study NZTA4007. Poster 331 at the 38th Annual Meeting of the Infectious Diseases Society of America, New Orleans, LA, Sept 7-18, 2000.
7. Rosenzweig, JC, Fischl, M, Kirkland, L, Tashima, K, Paar, D, Gensler, T, Capuano, G, and Hernandez, J. Compact triple nucleoside therapy can impact adherence in the prison setting. Poster 117 at the 5th Intl Congr on Drug Therapy and HIV infection, Glasgow, UK, 22-26 October 2000.
8. McClemon, DR, Gather, J, Thompson, M, Farthing, C., Fischl, M, Kirkland, L, Hessesenthaler, S, Shaefer, M, St Claire, M, Hernandez, J. Genotypic patterns after virologic failure following 24 weeks of triple nucleoside therapy in under-represented and incarcerated populations. Poster 361 at the 5th Intl Congr on Drug Therapy and HIV infection, Glasgow, UK, 22-26 October 2000.
9. *NEJM*, September 14, 2000; 343(11): 808-810, also available at <http://www.nejm.org/content/2000/0343/0011/0808.asp>.

CME IS NOW AVAILABLE ONLINE AT WWW.HIVCORRECTIONS.ORG:

As of Friday, December 22, you will be able to take HEPP News' continuing medical education (CME) tests online at <http://www.HIVcorrections.org>. Any internet browser will enable you to take the HEPP News CME tests every month. Your test results will be registered with the Brown Medical School Office for Continuing Medical Education. When you pass the test, you can either download your CME certificate from the website or request Brown to send the certificate in the mail. Try it out this week!

HIV IOI Treatment of STDs Commonly Seen with HIV

	TREATMENT	COMMENTS
Chlamydia Trachomatis	<ul style="list-style-type: none"> ■ Doxycycline* 100 mg po bid x 7 ■ Azithromycin 1 gm po x 1 ■ Ofloxacin* 400 mg po bid x 7 ■ Erythromycin base 500 mg po qid x 7 or EES 800 mg po qid x 7 	none
Herpes Simplex	<p><i>First episode</i> Genital Acyclovir 200 mg po 5x/day or 400 mg po tid or Famciclovir 250 mg po tid or Valacyclovir 1 mg po bid.</p> <p>All regimens should be given 7-10 days or until clinical resolution.</p> <p><i>Recurrent episodes</i> Immunosuppressed patients such as those with HIV can benefit from the use of Acyclovir.</p> <ul style="list-style-type: none"> ■ Acyclovir 200 mg po 5x/day x 5 days or 800 mg/po bid x 5 days or famciclovir 125 mg bid x 5 days or Valacyclovir 500 mg bid x 5 days. <p><i>Prophylaxis</i> Recommendations are (see comments):</p> <ul style="list-style-type: none"> ■ Acyclovir 400 mg po bid or ■ Valacyclovir 500 mg po qd or ■ Famciclovir 250 mg po bid or ■ 1 gm po qd or 250 mg po bid 	<p><i>First episode</i> Severe disease with proven or suspected Acyclovir resistant strains: Foscarnet 40 mg/kg IV q8h until clinical resolution. Cidofovir 1% gel qd x 5d may also be effective with Acyclovir-resistant HSV.</p> <p><i>Recurrent episodes</i> Treatment of HSV in the setting of HIV infection may require higher doses or more prolonged course of treatment.</p> <p><i>Prophylaxis</i> Safety and efficacy is documented for both frequency and severity of breakthrough episodes with continuous prophylaxis up to seven yrs (JID 1994;169:1338). Prophylaxis also reduces viral shedding between episodes. The usual indication is >6 episodes/year.</p>
Neisseria Gonorrhoeae	<p><i>a. Urethral, endocervical, rectal, pharyngeal</i></p> <ul style="list-style-type: none"> ■ Ceftriaxone 125 mg IM x 1 ■ Ciprofloxacin 500 mg po x 1 ■ Ofloxacin* 400 mg po x 1 ■ Cefixime 400 mg x 1 <p><i>b. Disseminated GC</i></p> <ul style="list-style-type: none"> ■ Ceftriaxone 1 gm IV or IM qd 	<p>Concurrent treatment of presumed <i>C. trachomatis</i>: Doxycycline* 100 mg po bid x 7 days or Azithromycin 1 gm po x 1</p> <p>Alternatives for Disseminated GC:</p> <ul style="list-style-type: none"> ■ Cefotaxime 1 gm IV q8h ■ Ceftizoxime 1 gm IV q8h or ■ Spectinomycin 2 gm IM q12h <p>Duration: Parenteral therapy until 24-48 hrs after symptoms resolve, then Cefixime 400 mg po bid or Ciprofloxacin* 500 mg po bid to complete >1 wk treatment</p>
Syphilis	<p>Primary, secondary, early latent (<1 year): Benzathine penicillin 2.4 mu IM x 1 Doxycycline 100mg po bid x 14 days</p> <p>Late latent or syphilis of unknown duration: Benzathine penicillin 2.4 mu IM q week x 3</p> <p>Neurosyphilis Penicillin G 18-24 mu IV qd, divided q4h x 10-14 days</p>	<p>Penicillin is drug of choice.</p> <p>Lumbar puncture recommended for late latent or syphilis of unknown duration (Some authorities recommend LP for all HIV positive patients with early syphilis either at outset or 6 months after therapy.)</p> <p>For Neurosyphilis, repeat LP is required every 6 months until CSF cell count is decreased</p>
Warts	<p><i>Provider-Administered Therapy</i></p> <p>Cryotherapy 60-97% clearance at 3-6 weeks 20-79% recurrence</p> <p>Podophyllin 19-80% clearance 23-70% recurrence Use only for <10cm² area Not for use in pregnant women</p> <p>Trichloroacetic acid & Bichloroacetic acid 50-100% clearance 6-50% recurrence</p>	<p><i>Patient Applied Therapy</i></p> <p>Podofilox 40-82% total clearance within 4-6 weeks 4-33% recurrences</p> <p>Imiquimod 37-85% total clearance 13-19% recurrences</p> <p>Cannot be used on mucosal surfaces</p>

*tetracycline, fluoroquinolones contraindicated in pregnancy

RESOURCES

National Public Radio's series on "The Price of Punishment"

Boston public radio station WBUR has produced a series of stories on prisons and jails in Massachusetts and nationwide. The series discuss various topics including the increasing number of women behind bars, the stresses of overpopulated prisons (MCI Framingham is currently 125% over capacity), and a few personal stories.

Visit their site online at <http://wbur.org/prison/women.shtml>.

National Commission on Correctional Health Care: Draft Recommended Correctional Clinical Guidelines

<http://www.ncchc.org/clinicaldrafts/index.html>

HUMAN RESEARCH PROTECTIONS WEBSITES:

Office for Human Research Protections (OHRP) (formerly Office for Protection from Research Risk, OPRR)

<http://ohrp.osophs.dhhs.gov/>

Food and Drug Administration

<http://www.fda.org>

Institutional Review Board Guidebook, 1993

http://ohrp.osophs.dhhs.gov/irb/irb_guidebook.htm

Code of Federal Regulations Title 45 Part 46 Protections for Human Subjects:

<http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>

STD WEBSITES:

CDC's Center for STD Prevention

<http://www.cdc.gov/nchstp/dstd/dstdp.html>

DHHS Treatment Guidelines

<http://www.hivatis.org>

MMWR 1998 Guidelines for Treatment of Sexually Transmitted Diseases

<http://www2.cdc.gov/mmwr>

Internet Grateful Med

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

Mediconsult

<http://www.mediconsult.com>

NEWS FLASHES

MMWR reports on 1999 TB Outbreak in South Carolina Prisons

Thirty-one cases of tuberculosis (TB) were confirmed among HIV-infected male inmates and parolees who had resided in the same dormitory designated for HIV-infected inmates in a South Carolina prison. The outbreak originated with an inmate who had infectious TB that was undiagnosed for at least two months. This outbreak demonstrates that the rapid spread of TB among incarcerated individuals and their health care providers can be a consequence of segregated housing for HIV-infected inmates. (CDC. MMWR 11/24/00; 49(46): 1041-1044).

Higher Prevalences of STDs Reported at STD Conference

For the first time in twenty years, Gonorrhea incidence is on the rise, according to CDC data presented at the National STD Prevention Conference, December 4-7, 2000, Milwaukee, WI. CDC's Ronald O. Valdiserri attributes the increase in part to better tests and more widespread screening. The national rate of gonorrhea infection is 133 cases per 100,000 people, 849 cases per 100,000 African Americans, 75 per 100,000 Hispanics, and 28 per 100,000 whites. The CDC reported that chlamydia is more common than both gonorrhea and syphilis, with 254 cases per 100,000 last year. Human papillomavirus is the most common STD, and strain HPV-16 is responsible for about half of all cervical cancers. The good news is, however, that syphilis cases continue to fall. The rate of infection is 2.5 cases per 100,000, and 79% of the country's 3,115 counties reported no new cases in 1999. (Brown, David. "Gonorrhea Decline Reverses: Cases Up 9%. Washington Post, www.washingtonpost.com).

New Formulations of Interferon-alfa better at fighting HCV

A new version of interferon alpha, "pegylated interferon," fights hepatitis C much better than its predecessor. Two recent reports in the New England Journal of Medicine compared Hoffmann-La Roche's "Pegasys" to the company's standard interferon, Roferon-A

(Zeuzem S, Feinman V, Rasenack J et al. JAMA 12/7/00; 343(23):1666-72; and Heathcote J, Shiffman M, Cooksley G. JAMA 12/7/00; 343(23):1673-80.). Schering also has a new formulation, "peginterferon," which recently received Health Canada's approval for marketing. Pegylated interferon is interferon that has polyethylene glycol attached to it. Polyethylene glycol reduces the elimination of interferon from the body, which allows for once-weekly dosing in both Schering and Roche's forms of the drug. Both forms of pegylated interferon are also pending approval in the United States. (Schagger D, Sorrell M. Editorial. 12/7/00; 343(23): 1723-24.)

FDA Approves Trizivir (ABC/AZT/3TC)

The FDA has approved Trizivir for the treatment of HIV in adults and adolescents. The recommended dose is one tablet twice a day. Each dose of Trizivir is a fixed-dose combination of Ziagen (abacavir/ABC), Retrovir (zidovudine/AZT), and Eпивir (lamivudine/3TC), three nucleoside reverse transcriptase inhibitors (NRTIs) already approved by FDA. Trizivir is not recommended for treatment in adults or adolescents who weigh less than 40 kilograms because it is a fixed-dose tablet. It may be used alone or in combination with other antiretroviral agents for the treatment of HIV infection, but should not be administered concomitantly with abacavir, lamivudine, or zidovudine, which are already contained in Trizivir. Healthcare providers and patients should be aware of the serious and sometimes fatal adverse event of hypersensitivity caused by abacavir (see HEPP News, April 1999). Ziagen and Trizivir both contain abacavir and neither of these drugs should be taken by someone who may have experienced symptoms of a hypersensitivity reaction to abacavir.

An Abacavir Hypersensitivity Registry has been established. Physicians should register patients by calling 1-800-270-0425. Trizivir is manufactured by Glaxo Wellcome, Research Park Triangle, N.C. (Full report available at <http://www.fda.gov/bbs/topics/answers/ans01053.html>)

SAVE THE DATES

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

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
Visit: www.retroconference.org

13th National HIV/AIDS Update Conference

March 20-23, 2001
San Francisco CA
Call: 212.806.1633
Fax: 212.806.1608
Visit: www.amfAR.org

Clinical Updates in Correctional Health Care 6th Semi-Annual Spring Educational Conference

May 5-8, 2001
Las Vegas, Nevada
Sponsored by NCCHC and ACHP
Call: 773.880.1460
Fax: 773.880.2424
Visit: <http://www.ncchc.org/conference/clinical.html>

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CME is now available ONLINE at www.hivcorrections.org

1. Which of the following statements are true about the laboratory evaluation of syphilis in an HIV infected patient?

- a) HIV does not alter the laboratory evaluation of syphilis.
- b) Evaluation consists of non-treponemal screening tests (RPR or VDRL).
- c) A positive evaluation should be confirmed with specific treponemal tests (MHA-TP, TPHA, or FTA).
- d) b and c
- e) all of the above

2. An HIV patient receiving treatment for syphilis should undergo repeat serologic testing to monitor the patient's response to syphilis therapy. How often should serologic testing be performed?

- a) 3, 6, 9, 12 and 24 months after treatment.
- b) Every 6 months until CSF cell count is decreased.
- c) Every 6 months for two years
- d) b and c

3. Which of the following statements are true concerning Herpes simplex (HSV) in an HIV infected patient?

- a) Acyclovir resistance can occur in patients with HIV associated immunosuppression.
- b) Because response to therapy can be delayed, HSV treatment should be continued beyond the standard 10 days if ulcers have not healed or if new lesions continue to appear.
- c) Foscarnet may be used to treat resistant virus.
- d) b and c
- e) all of the above

4. CDC guidelines recommend that which of the following populations of women should be screened for chlamydia infection?

- a) sexually active women under 20
- b) women 20-24 with more than one sexual partner in the preceding 60 days
- c) women 20-24 with a history of inconsistent use of barrier contraception
- d) b and c
- e) All of the above

5. What percentage of chlamydia cases are asymptomatic?

- a) >80%
- b) 50%
- c) >40%
- d) 35%

6) Which of the following STDs may cause pelvic inflammatory disease among women?

- a) Syphilis
- b) Trichomonas
- c) Human Papillomavirus (HPV)
- d) Gonorrhea
- e) b and c
- d) All of the above

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
CTC Updates	5 4 3 2 1	5 4 3 2 1
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2. Do you feel that HEPP News helps you in your work? Why or why not?

3. What future topics should HEPP News address?

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