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INFECTIOUS DISEASES IN CORRECTIONS REPORT

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ABOUT IDCR

IDCR, a forum for correctional problem solving, targets correctional physicians, nurses, administrators, outreach workers, and case managers. Published monthly and distributed by email and fax, IDCR provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, as well as efficient ways to administer treatment in the correctional environment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education. IDCR is distributed to all members of the Society of Correctional Physicians (SCP) within the SCP publication, CorrDocs (www.corrdocs.org).

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DILEMMAS IN THE CARE OF THE HIV-INFECTED INCARCERATED INDIVIDUAL

*By David Alain Wohl, MD**
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DISCLOSURES: *Speakers Bureau: Gilead Sciences, Abbott Laboratories, Boehringer Ingelheim, Bristol Myers Squibb; Grant Support: Abbott Laboratories, Roche Pharmaceuticals, NIH*

To say that the management of HIV infection in prisons and jails is different than that in the free world would be a great understatement. The challenges faced by correctional health care providers in delivering high quality HIV care are myriad and generally include the constraints that accompany working within a system designed primarily to meet security, rather than medical needs. Budgetary restraints, a patient population that suffers disproportionately from mental and physical co-morbidities and less-than-ready access to subspecialty experts further complicates care of these patients.

What follows is a series of fictional clinical cases that reflect familiar dilemmas correctional clinicians caring for HIV-infected patients encounter. Each case is accompanied by a discussion of potential options clinicians may consider.

Case 1. The Treatment-Experienced Patient Entering Prison Off of Antiretroviral (ARV) Therapy

Wayne R entered state prison after a three-month stay at the county jail. He first learned he was HIV-infected four years prior, when incarcerated in another state facility, and was placed on HIV therapy. He cannot remember the names of the medications he was previously given, but believes some of them were "blue-ish". Between incarcerations he admits he was intermittently adherent to his medication regimen, but rarely took any of his medications during the past 12 months.

Upon entry to the county jail, Wayne R's CD4 T-cell count was 387 cells/mm^3 and viral load was 76,800 copies/mL. He did not complain of symptoms that could be ascribed to HIV infection and his weight increased during his incarceration. Upon entry to prison, basic HIV-related laboratory tests were repeated. At this time, his CD4 T-cell count was 359 cells/mm^3; viral load was 94,900 copies/mL. A genotype resistance test was completed and demonstrated no evidence of reduced susceptibility of the virus. Jail medical records did not reveal Wayne R's ARV treatment history. A request for medical information accompanied by a release of information signed by the patient was sent to the out-of-state prison and after six weeks of repeated efforts, including a call to the facility, records were obtained. These records revealed that the patient had a CD4 T-cell count of 223 cells/mm^3 when HIV was initially diagnosed and had been given an ARV regimen containing zidovudine/lamivudine (Combivir®) and nelfinavir.

Approximately three months after the patients' arrival, his CD4 T-cell count was repeated and was 312 cells/mm^3. At this time, the patient complained only of increased fatigue. His clinician wanted to restart HIV therapy (and the patient agreed) but the clinician was unsure whether to reinitiate the medication regimen the patient had previously been given or craft a new combination using agents that are unlikely to be affected by the resistance mutations the patient may have cultivated, but were not detected on resistance testing.

Discussion: Correctional clinicians often find themselves working in a "data vacuum". Inmate patients can be poor historians of their prior medical care and requests for information from

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outside institutions, despite releases of information, frequently go unheeded. In this case, records were procured, but only after persistence by the medical staff. Often, follow-up telephone calls to clinics and hospitals have to be made to obtain needed medical information. Medication data may also be obtained by contacting community pharmacies the patient used while not incarcerated.

In many cases, prior medication history is simply not available. Targeted questioning of the patient may provide helpful clues as to what medications the patient has taken and which medications, due to resistance, may be likely to be ineffective. To determine if the patient ever took efavirenz, a popular and potent non-nucleoside reverse transcriptase inhibitor (NNRTI), which can be rendered essentially ineffective with the rapid development of few mutations, the patient can be asked if he ever took gold-colored medication at night that produced vivid dreams. Prior NNRTI experience in a patient with poor adherence would raise concern about NNRTI resistance. Likewise, asking if a medication needed to be refrigerated would help determine if ritonavir or lopinavir/ritonavir (LPV/r) (Kaletra®) were previously prescribed. This patient recalled his pills were blue. If he also remembered that he needed to take five pills twice a day and had some diarrhea when on the medication, one could assume he had received nelfinavir.

In some cases, patients may recall nothing about their medications. In such situations, starting a regimen that is most likely to be effective despite prior treatment is prudent when HIV therapy is indicated. Ritonavir-boosted protease inhibitors (PIs) may be effective in this circumstance, as resistance is unusual when such a combination is used and there can be activity of the combination even in the setting of prior protease inhibitor (PI) resistance.

After obtaining the patients' treatment history, the clinician was confronted with the choice of restarting the original regimen or prescribing a new combination. The patients' intermittent adherence places him at high risk for drug resistance. This is difficult to document now that he has been off therapy, as wild-type virus (not resistant) will generally outgrow resistant virus once the selective pressure of medication is removed. A notable exception is the persistence of NNRTI resistance mutations despite discontinuation of the NNRTI, yet some assumptions can be made. The first mutation the patient may have acquired is the M184V mutation, conferring high-level resistance to lamivudine (3TC) and emtricitabine (FTC). With on-going suboptimal adherence to zidovudine (ZDV), thymidine analogue mutations emerge. Thymidine analogue mutations lead to cross-resistance to most of the nucleoside reverse transcriptase inhibitors (NRTIs). In the worst-case scenario, mutations that reduce susceptibility to inhibitors of the HIV-1 protease would have been selected. Classically, nelfinavir resistance develops with the D30N mutation, which leads to limited cross-resistance to other agents in this (ARV) class but can be followed by more damaging mutations that threaten the effectiveness of this class of medications.

At this time, determining which medications this patient actually took is reduced to guesswork. Assuming the worst-case dual ARV class resistance, the clinician would be faced with the challenging task of designing a salvage regimen. There is little attraction in restarting the original nelfinavir-based regimen, given it is relatively inconvenient and demonstrated to be inferior to more commonly used initial regimens.

An alternative strategy would be to recommend to the patient that he simply restart Combivir® and nelfinavir temporarily for a period of four weeks, at the end of which a repeat in CD4 T-cell count and viral load can be drawn along with a test of viral resistance. The goal here is to apply short-term selective pressure with this regimen so that resistant virus present in low concentrations can outgrow wild type virus and become readily detectable upon resistance testing. Four to six weeks of therapy with this regimen should flush out resistant strains, but be unlikely to lead to any further resistance. The resistance test results can then be applied to direct decision-making. For example, demonstration of only the M184V mutation would be reassuring and suggest a regimen containing ritonavir-boosted PI plus tenofovir and ZDV would likely be potent. Some would also add FTC or 3TC to preserve the M184V mutation, as it has been associated with reduced ability of the virus to replicate.[1] The presence of NRTI mutations in addition, would indicate a more novel approach is needed and the combination of a ritonavir-boosted PI and a NNRTI may be required. Although such a genotype might indicate that the virus remains susceptible to both tenofovir and didanosine, there is mounting evidence that this pairing blunts CD4 T-cell count increases and, when coupled with a NNRTI, leads to suboptimal viral suppression.[2, 3] Much less likely, but possible, would be the documentation of multi-class drug resistance with thymidine analogue mutations, NNRTI and multiple PI mutations. In this situation, aggressive multi-drug salvage therapy including a boosted PI (i.e. lopinavir or tipranavir) would be indicated to reverse decreasing CD4 T-cell counts.

When forced to make a decision with limited available data, the clinician can be aggressive in obtaining outside records and wisely apply understanding of the dynamics of viral resistance to detect hidden mutations before assuming the worst and embarking on a new regimen that would likely be costly and challenging for this patient.

Case 2. The HIV and Hepatitis B Virus (HBV) Co-Infected Patient

Sylvia G was screened for HIV infection soon after she arrived at prison. She was found to be HIV seropositive. Follow-up testing revealed a CD4 T-cell count of 567 cells/mm^3 and HIV viral load of 14,500 copies/mL. Additionally, she had active HBV infection evidenced by presence of hepatitis B surface antigen (HBsAg). Antibodies for hepatitis C virus (HCV) were negative, hepatitis B e antigen (HBeAg) was positive, HBV DNA PCR level was 6.8 x 108 IU/mL and ALT level was 2.8 times the upper limit of normal. The patient has no evidence of cirrhosis on physical examination; albumin and synthetic liver function parameters are within normal limits. The patient asks whether she needs to be treated for her HIV and HBV infections and, if so, how? She will be in prison for approximately 18 months.

Discussion: HBV infection typically receives less attention than HCV, particularly in the setting of HIV co-infection. The lack of attention on this important pathogen was reflected in a recent Wall Street Journal editorial titled "Hepatitis B: The Forgotten Virus". Although less common than HCV co-infection, the prevalence of HBV infection is high among HIV-infected persons (approximately 10%) as well as in the general prison population (13%-47%).[4] Furthermore, HBV can be a significant cause of liver disease in the setting of HIV infection. Screening of all HIV-infected individuals for active HBV infection is an important aspect of HIV preventive care and can be accomplished by testing for the presence of HBsAg.

A remarkable boon to the therapeutic management of HIV/HBV co-infection is the existence of agents that are active against both viruses. Tenofovir, 3TC and FTC all have anti-viral activity against both HIV and HBV. Although none of these medications are specifically approved by the Food and Drug Administration (FDA) for the treatment

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of chronic HBV in the HIV-infected patient, the dual activity of these antivirals has permitted simultaneous treatment of both viruses with standard HIV regimens (i.e. 3TC, FTC, efavirenz). Indeed, when ARV therapy is indicated for HIV/HBV co-infected patients, inclusion of one or more drugs active against HBV in the regimen is recommended.[5, 6] Some authorities recommend that tenofovir be used preferentially, in combination with FTC or 3TC, for patients requiring treatment of both HIV and HBV.[7] The use of tenofovir in such patients has been advocated, despite the black box label warning on this ARV that states it is not indicated for the treatment of chronic HBV and that acute exacerbations of hepatitis can occur in individuals who discontinue the drug. Similar warnings can be found for other dually active NRTIs.[1]

There is less clarity regarding the best approach to take when there is no indication for the initiation of HIV therapy (i.e. when CD4 T-cell count is high). Use of 3TC, FTC or tenofovir alone, or when paired, risks development of HIV resistance to these agents, limiting their future use. In cases when CD4 T-cell count approximates the HIV treatment threshold of 350 cells/mm^3 and/or when HIV viral load is very high, some clinicians justify initiating a regimen to treat both viruses. Alternatively, adefovir, a nucleotide analogue that is FDA-approved for the treatment of HBV in HIV-uninfected patients, can be dosed to have activity against HBV and not HIV - running no risk of incurring HIV drug resistance. Adefovir also has activity against 3TC-resistant HBV.

Another option was recently introduced with the approval of entecavir (Baraclude®), a nucleoside analogue that is potent against HBV and has no antiviral activity against HIV. Entecavir was FDA-approved this year for the treatment of HBV mono-infection and for HIV/HBV co-infection in patients with prior 3TC experience.

In this case, Sylvia G meets criteria for HBV treatment. She has active HBV as demonstrated by HBV serologies and viral load, as well as hepatic inflammation as evidenced by hypertransaminasemia; she has no signs of cirrhosis on physical examination or laboratory testing. It is difficult to justify treatment for her HIV given her high CD4 T-cell count and relatively low HIV viral load. Therefore, she should be treated with an antiviral that has activity against HBV, but that will not risk HIV ARV resistance. At present, adefovir is the best option. The role of entecavir in such patients needs further study.

Case 3. Acute HIV Infection

Bruce S came to sick call asking to be tested for HIV infection. He states he was playing basketball six weeks prior and during a valiant attempt at rebounding, collided with another inmate whose front teeth cut into Bruce S's scalp. According to the patient, there was blood from the opposing player's mouth and his own scalp following the collision, but that this incident went unreported. When he heard a rumor that the other player is HIV positive, which the clinical staff does not confirm to Bruce S but knows to be the case, he asked to get tested for HIV. According to the medical record, Bruce S had been HIV tested one year prior upon prison entry and was seronegative.

On examination, a linear puncture wound was observed on the scalp with surrounding erythema and some pus evident. Appropriate wound care and oral antibiotics were administered. Blood was drawn for HIV antibodies, HIV viral load, HBV and HCV serologies. All test results were negative. Approximately six weeks later, the HIV antibody test was repeated. This time the test was positive and the confirmatory Western blot indeterminate with three bands reactive (p24, p40 and p55), suggesting evolving HIV seroconversion. The surprised clinician ordered a follow-up viral load, which returned at 350,000 copies/mL and a subsequent genotypic resistance test report demonstrated no viral resistance mutations. On further questioning, Bruce S indicates that following the incident on the basketball court he "may have" had unprotected consensual sex with another inmate.

The clinician caring for Bruce S is familiar with the U.S. Department of Health and Human Services (DHHS) guidelines on the treatment of HIV-infected adults and adolescents.[5] These guidelines describe the potential risks and benefits of treatment during acute HIV infection. The clinician telephones an HIV specialist at a nearby academic hospital for advice regarding whether to initiate ARVs. The specialist feels that treatment is likely to be beneficial during acute infection but admits to only seeing a handful of cases of acute HIV, all of which have entered clinical studies.

Discussion: Opportunities to detect acute infection may be more abundant in correctional settings where HIV transmission risk behaviors are not rare and HIV testing is usually accessible. Yet, detection of acute HIV infection requires consideration of the diagnosis when presented with a patient with a consistent history. The diagnosis is a challenge to make, as the presenting symptoms of acute HIV infection are usually non-specific. Fever, lymphadenopathy, pharyngitis and/or rash are the most common findings on presentation. In some cases, encephalitis, rhabdomyolysis and opportunistic infections may be seen; however, these are rare. Given the nature of the presenting symptoms, the clinician must carefully probe for potential risky exposures in the weeks prior when examining a patient with consistent symptoms, much like we ask about tick exposures and sick contacts in patients with febrile illnesses.

In this case, the patient presented with his own concerns regarding a potential exposure. However, despite experiencing an injury that could have led to HIV transmission, albeit a fairly low risk injury, laboratory testing and detailed history-taking revealed the patient did indeed recently acquire HIV, though probably via a more customary route than a defensive foul. Had he acquired HIV from the collision with the HIV-infected basketball player, his HIV viral load should have been detectable and high over six weeks later when he first presented. Likewise, his HIV antibody tests would have been expected to demonstrate at least evolving seroconversion rather than be completely negative.

Converging data suggest that during the acute phase of HIV infection, when the viral load in the blood and genital secretions are at their highest, the patient is most likely to transmit virus to others.[8] Therefore, an essential aspect of the management of acute HIV infection includes counseling the patient regarding risk behaviors as well as contact tracing of recent sexual, needle sharing and tattoo equipment sharing partners.

The clinicians' dilemma as to whether to prescribe ARV therapy in this case is shared by those working outside of prisons and jails. An aim of correctional health care providers is to administer medical care that is on par with the standard of care that exists in the community. However, the community standard of care can sometimes be ill-defined, variable by community or developing as new data emerge. In the case of acute HIV infection, treatment with ARVs is common in some quarters, but at present, cannot be considered standard practice. The benefits of such early therapy remain mostly theoretical and include potential preservation of HIV-specific immune function, possible lowering the viral load set point and reduction in the transmissibility of the virus. Downsides include exposure to treatment without previously proven clinical benefit, the potential toxicity of therapy, the risk of drug resistance and cost. As stated in the DHHS

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IDCR Spotlight: Highlights of the 2005 Annual NCCHC Meeting

Joseph Paris, MD, PhD, Medical Director, Georgia Department of Corrections*
Courtney Colton Managing Editor IDCR*
***DISCLOSURES:** Nothing to disclose*

The 2005 annual Conference of the National Commission on Correctional Health Care (NCCHC) took place on October 8-12, 2005 in Denver, Colorado. This annual meeting is one of the most important gatherings of correctional health care providers. Prior to the conference, IDCR hosted its' 9th annual pre-conference symposium. Despite competition from four other pre-conference symposiums, there was standing room only throughout IDCR's sessions.

A short review of the IDCR symposium is presented here, for those who were unable to attend.

David Thomas, MD, JD (Professor and Chairman, Department of Surgery, Division of Correctional Medicine, NovaSoutheastern University) provided an overview on legal and ethical dilemmas many correctional health care providers face when treating hepatitis C virus (HCV)-infected inmates. Joseph Bick, MD (Director, HIV Treatment Services, California Medical Facility, California Department of Corrections) spoke on infection control within the correctional setting, illuminating a number of barriers to cleanliness that impact on the transmission of infections in prisons and jail. Anne DeGroot, MD (Co-Chief Editor IDCR, Brown University) provided an update on HIV treatment recommendations for incarcerated women and presented on HCV for Bill Cassidy, MD (Associate Professor of Medicine, Louisiana State University Health Sciences Center), who was unable to attend the conference. David Paar, MD (Associate Professor of Medicine and Director of HIV Care for the University of Texas Medical Branch at Galveston) concluded the IDCR pre-conference seminar with a discussion on 2005 changes to the HIV treatment guidelines.

These issues are important to address because high-risk behaviors prevalent among the incarcerated population combined with the limited access to health care prior to incarceration and poor health care education, conspire to pose a formidable challenge to public health. The correctional setting offers an unparalleled opportunity to test, diagnose, educate and treat these patients. The IDCR experts focused on programs successfully integrated into the correctional setting. An enthusiastic audience peppered the experts with pertinent questions, and by the end, many stated that they wished there had been even more time for questions. After the seminar, everyone had a chance to visit the new IDCR booth which drew a stream of visitors throughout the NCCHC conference breaks.

The conference continued with a well-attended Society of Correctional Physicians (SCP) conference on Sunday, October 9th. Death in restraints, mortality reviews, primary ENT and eye care were topics presented by qualified speakers. The SCP is a sister organization of the IDCR and bundles IDCR publications into its quarterly newsletter, CorrDocs.

The NCCHC opening ceremony on Monday, October 10th featured a Keynote Address by IDCR board member, Louis Tripoli, MD, (Vice President of Medical Affairs, CMS) who regaled the audience with his touching adventures as a correctional physician in exotic locations including Fallujah, Abu Ghraib and other, equally dangerous Iraqi locales. The following three days were a whirlwind of concurrent breakout sessions in multiple tracks, including administration, infectious disease, juvenile, legal, medical, mental health, nursing, dental and professional development.

IDCR board members also presented seminars during the conference proper. David Paar, MD discussed methadone maintenance and harm reduction in state and federal prisons. Joseph Paris, MD, PhD spoke on using ALT levels to determine HCV treatment eligibility and Neil Fisher, MD (Medical Director, Chief Health Officer, Martin Correctional Institute) gave a presentation on the rapidly changing field of HIV medicine during one of the educational breakfasts. Of note, Eric Avery, MD delivered a seminar regarding overcoming mental health barriers in the treatment of HIV-infected incarcerated persons and John Maye, MD discussed prison health in developing countries. Drs. David Paar and David Thomas also delivered lectures during the conference proper similar to those which they presented during the IDCR pre-conference symposium.

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guidelines, the clinician must consider the evidence supporting early treatment and the risks involved. That the guidelines do not definitively recommend ARV therapy during acute infection does not mean it should not be considered. In fact, the guidelines leave it as an option for the clinician to consider.

In this case, the clinician sought to learn the community's practices regarding the management of acute HIV infection. The clinician has also read the relevant guidelines. A discussion with the patient regarding the risks, benefits and alternatives to ARV therapy should follow. Together, weighing the available data, an educated decision can be made. If therapy is initiated, ARVs used for patients with chronic HIV infection who are initiating therapy can be employed. Follow-up should include HIV viral load testing and toxicity monitoring. The optimal duration of therapy following acute HIV infection is not known. Most clinicians discontinue HIV therapy initiated during acute infection after six to 18 months. Further data regarding the optimal management of acute HIV infection and the duration of HIV treatment in this situation are expected to emerge from on-going clinical studies.

Case 4. Multi-Drug Resistant (MDR) HIV

Upon jail intake, Carrie R was very sick. She had been abusing crack cocaine heavily and had not been taking her ARVs or Pneumocystis carni pneumonia (PCP) prophylaxis as her health department physician's assistant (PA) had prescribed. Within three days of her arrest, she was transferred to the local hospital with fever and shortness of breath. PCP was diagnosed, CD4 T-cell count was 13 cells/mm^3 and an HIV viral load would eventually return at 86,000 copies/mL. After recovering from PCP, the patient was transferred back to the jail.

Before hospital discharge the patient was started on LPV/r and Combivir®, which she had been on previously. A genotypic resistance test was performed and demonstrated multiple thymidine analogue mutations including 41L, 118I, 210W, 215Y as well as 184V plus 103N (a class-killing NNRTI

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mutation) and a series of PI mutations including 10I, 30N, 36I, 74S and 90M that suggest decreased response to most PIs.

The patient has longstanding HIV infection and was first treated with stavudine (d4T) and 3TC. Later she was treated with d4T, 3TC and nevirapine. She also thinks she may have been treated with a medicine that can cause kidney-stones (i.e. indinavir) and also nelfinavir, but is uncertain. She recognizes the old formulation of didanosine from a picture of the medication on a drug company guide to ARVs. She states she was switched to LPV/r and Combivir® approximately six months ago, upon returning to a clinic after falling out of care.

The PA discusses the results of the latest genotype with the patient, who states this episode of pneumonia was frightening and that she never wants to go through another bout of PCP again. She is supposed to remain in jail for approximately eight weeks and will likely be transferred to the state prison following her trial.

Discussion: Treatment of the patient with MDR HIV infection is one of the most daunting challenges confronting HIV health care providers. Often, as in this case, resistance has been cultivated during repeated bouts of non-adherence - often fueled by substance abuse, mental illness and other causes of personal chaos. When faced with a genotype report that has more red ink than black, the clinician and patient must have a frank discussion about what the patient feels she is capable of and willing to do to forestall HIV progression. Incarceration may be an optimal time to engage in such a discussion as the patient will be free from substance abuse, may be getting appropriate treatment of underlying depression or other mental illness and can be monitored closely.

The aims of therapy must be made clear. Attempting to suppress the HIV viral load to undetectable levels may no longer be a realistic goal. Instead, therapy that can impede the virus in its CD4 T-cell count destruction should be employed to slow disease progression and stall for time as newer therapies are developed. Therapeutic management of multi-drug resistance involves two complimentary approaches: application of new agents that are likely to have antiviral activity against the virus and use of drugs to which the virus is resistant, but that reduces the ability of the virus to replicate.

Enfurvitide (T-20) and tipranavir are newer agents that are almost exclusively prescribed as part of "salvage" regimens. T-20 is an injectable HIV entry inhibitor. Its use in jails and prisons can be problematic, given it requires injection and is expensive, even by HIV treatment standards. Tipranavir is a PI that has been found to be more effective among patients with MDR HIV infection than optimized background therapy.[9] These data demonstrate that tipranavir is most effective when combined with T-20 in patients who have not previously taken T-20. Tipranavir requires boosting with 400 mg of ritonavir daily. Abbott Laboratories supplies this dose of ritonavir for use with tipranavir at no cost. A series of mutations have been described that reduce the activity of tipranavir. Guidelines on the use of tipranavir have been drafted by the American Academy of HIV Medicine (AAHIVM).[10]

In addition to the initiation of novel therapies, recycled ARVs or continuation of drugs to which the virus is resistant, are often included in salvage regimens. Some mutations, particularly against NRTIs, appear to reduce viral fitness and may provide clinical benefit when maintained. Examples of this effect have been described with 3TC and NRTIs.[1] The operative theory here is that highly mutated virus is defective, less able to replicate and less able to deplete CD4 T-cells. There has been no significant effect of maintaining NNRTIs when resistance to this class of ARVs is present.

In this case, the PA and the patient discussed the need for aggressive HIV therapy. The patient again stated her commitment to "whatever it takes" to get well. After consultation with an HIV specialist and the medical director of the jail, the PA prescribed tipranavir/ritonavir, T-20, tenofovir, FTC and ZDV - an aggressive and expensive option that may not be available in many jails.

Conclusion

Correctional clinicians have unique institutional barriers when interacting with their patients. However, these clinicians also have unique opportunities; the cluster of individuals with a history of high-risk behaviors is an opportunity for both clinical and behavioral intervention. The cases studies above can also include the opportunity to provide education regarding: 1) basic disease/infection information; 2) the importance of treatment adherence, including access to treatment upon release; 3) further education and support for disclosure to previous partners for follow-up counseling and testing, if and when appropriate and, at every opportunity; 4) behavioral risk/harm reduction.

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Editors Note:

I There may be considerable liability when treating a disease with a medication that has not been indicated for that purpose.

Letter from the Editor

Dear Correctional Colleagues:

This month, IDCR focuses on common dilemmas in the care of the HIV-infected incarcerated individual. Dr. David Wohl reviews four common scenarios faced by HIV-infected inmate patients and their clinicians: the treatment-experienced patient entering prison off of antiretroviral therapy, the HIV and hepatitis B virus co-infected patient, acute HIV infection and multi-drug resistant HIV.

Dr. Wohl points out that these common dilemmas are made more challenging given the constraints that exist in jails and prisons. Correctional clinicians must often seek creative solutions to meet the needs of their incarcerated patients. We believe that IDCR continues to serve an important role in disseminating these "best practice" solutions to our colleagues who work behind bars.

Also in this issue, Dr. Joseph Paris and IDCR managing editor Courtney Colton review the highlights of this autumn's annual Conference of the National Commission on Correctional Health Care, which took place in October in Denver, Colorado. This annual meeting is one of the most important gatherings of correctional health care providers.

This month's HIV101 provides a table of currently available antiretroviral (ARV) agents, with comments on the advantages and disadvantages of each ARV class.

At the end of this issue, readers should be familiar with some of the dilemmas faced in correctional healthcare and how to best tackle these dilemmas. Readers should also be familiar with preferred and alternative regimens for the initial treatment of HIV.

I would like to take this opportunity to extend our gratitude to Dr. David Thomas, who has served this past year as IDCR's Co-Chief Editor. We appreciate Dr. Thomas' long-term commitment to the health of the incarcerated, and thank him for the fine job that he has done for IDCR this past year. Dr. Wohl, an active member of IDCR's Editorial Board, has agreed to step up and manage content for 2006. Dr. Wohl is an Associate Professor of Medicine, Division of Infectious Diseases, University of North Carolina, and is Co-Director of HIV Services for the North Carolina Department of Corrections. We all look forward to working with Dr. Wohl during this coming year to ensure that IDCR continues to meet the educational needs of our correctional colleagues around the world.

Sincerely,

Joseph Bick*

**Nothing to Disclose*

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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.

HIV101: Initial Treatment: Preferred Regimens

NNRTI-Based	# pills/day
Efavirenz* + (lamivudine [3TC] or emtricitabine [FTC]) + (zidovudine [AZT, ZDF] or tenofovir DF [TDF])	2-3

PI-Based	# pills/day
Lopinavir/ritonavir (Kaletra®) + (lamivudine [3TC] or emtricitabine [FTC]) + (zidovudine [AZT, ZDF])	8-9

HIV101: Initial Treatment: Alternative Regimens

NNRTI-Based	# pills/day
Efavirenz* + (lamivudine [3TC] or emtricitabine [FTC]) + (abacavir [ABC] or didanosine [ddI] or stavudine [d4T])	2-4
Nevirapine** + (lamivudine [3TC] or emtricitabine [FTC]) + (zidovudine [ZDV] or stavudine [d4T] or didanosine [ddI] or abacavir [ABC] or tenofovir [TDF])	3-6

PI-Based	# pills/day
Atazanavir + (lamivudine [3TC] or emtricitabine [FTC]) + (zidovudine [ZDV] or stavudine [d4T] or abacavir [ABC] or didanosine [ddI]) or (tenofovir [TDF] + ritonavir [RTV] 100mg/d)	3-6
Lopinavir/ritonavir (Kaletra) + (lamivudine [3TC] or emtricitabine [FTC]) + (stavudine [d4T] or abacavir [ABC] or tenofovir [TDF] or didanosine [ddI])	7-10
Fosamprenavir or fosamprenavir/ritonavir or indinavir/ritonavir or nelfinavir or saquinavir (hard- or soft-gel capsule)/ritonavir + (lamivudine [3TC] or emtricitabine [FTC]) + (zidovudine [ZDV] or stavudine [d4T] or abacavir [ABC] or tenofovir [TDF] or didanosine [ddI])	5-15

NRTI-Based	# pills/day
Abacavir [ABC] + lamivudine [3TC] + zidovudine [ZDV]^	2

**Avoid in pregnant women and women with high pregnancy potential.*

***Because of higher rates of hepatotoxicity, nevirapine should not be initiated in women with pre-nevirapine CD4-T cell counts less than 250 cells/mm^3 or men with CD4-T cell counts less than 400 cells/mm^3, unless the benefit clearly outweighs the risk.*

^To be used only when a preferred or alternative NNRTI- or PI-based regimen cannot or should not be used as first-line theapy.

Tables adapted from DHHS. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. October 6, 2005. Last accessed November 16, 2005 from http://aidsinfo.nih.gov/guidelines/default_db2.asp?id=50

Save the Dates

13th Annual Conference on Retroviruses and Opportunistic Infections
February 5-9, 2006
Denver, Colorado
Visit:
www.retroconference.org

13th Annual Ryan White National Youth Conference on HIV/AIDS
February 18-20, 2006
Philadelphia, PA
Visit:
www.napwa.org/rwnyc/

National Conference on African-Americans and AIDS
February 27-28, 2006
Philadelphia, PA
Visit:
www.minority-healthcare.com/

Updates in Correctional Health Care
April 8-11, 2006
Las Vegas, Nevada
www.ncchc.org

ACHSA 2006 Multidisciplinary Training Conference
May 11-13, 2006
Durham, North Carolina
http://achsa.org

XVI International AIDS Conference
August 13-18, 2006
Toronto, Canada
Visit: www.aids2006.org

REFRENCES:

DHHS. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. October 6, 2005. Available at http://aidsinfo.nih.gov/Guidelines/GuidelineDetail.aspx?MenuItem=Guidelines&Search=Off&GuidelineID=7&ClassID=1

DHHS. Guidelines for treating opportunistic infections among HIV-1 infected adults and adolescents. December 17, 2004. Available at http://aidsinfo.nih.gov/Guidelines/GuidelineDetail.aspx?MenuItem=Guidelines&Search=Off&GuidelineID=14&ClassID=4

CDC. Prevention and control of infections with hepatitis viruses in correctional settings. MMWR. 52(RR01):1-33.

News and Literature Reviews

Resistance Testing for Naïves is Cost-Effective
Utilizing a previously published model of HIV disease, Sax, et al, projected the long-term and clinical cost outcomes for a cohort of HIV-infected, antiretroviral (ARV)-naïve patients who undergo pretreatment resistance testing. In the base case, the overall prevalence of ARV resistance among treatment-naïve patients was 8.3%. Direct costs of treatment for both routine medical care and for acute illnesses were estimated from data from the AIDS Cost and Services Utilization Survey. In the absence of primary resistance testing, patients had a projected mean quality-adjusted life expectancy of 168.3 months and a total lifetime cost of $336,000. With resistance testing at the time of initial diagnosis, the mean quality-adjusted life expectancy increased to 169.3 months and total costs increased to $338,600. Study authors concluded that resistance testing at the time of HIV diagnosis is a cost-effective strategy that can lead to selection of a more effective initial ARV regimen and likely longer survival for patients who have drug-resistant virus.
Sax P, et al. Should resistance testing be performed for treatment-naïve HIV-infected patients: a cost-effectiveness analysis. Clin Infect Dis. 2005; 41(9):1316-23.

HPV Vaccine in Phase III Clinical Trials
GARDASILTM, a quadrivalent human papillomavirus virus (HPV) type 6, 11, 16, 18 recombinant vaccine, has been evaluated in a Phase III study, titled FUTURE II. Over 12,000 women, aged 16 to 26 years, at 90 centers were randomized to receive a three-dose regimen of either GARDASIL or placebo at day 1, month 2 and month 6. Among women who received three doses of GARDASIL, 100% of high-grade cervical pre-cancers and non-invasive cervical cancers (CIN 2/3 and AIS) associated with HPV types 16 and 18 were prevented. Twenty-one cases of CIN 2/3 or AIS were observed in the placebo group. This trial is part of the ongoing phase III program for GARDASIL, which involves over 25,000 people in 33 countries worldwide.
Finn S, et al. Prophylatic quadrivalent human papillomavirus (HPV) (types 6, 11, 16, 18) L1 virus-like particle (VLP) vaccine (GardasilTM) reduces cervical intraepithelial neoplasia (CIN) 2/3 risk. Oral abstract LB-8a. Infectious Diseases Society of America meeting. San Francisco, CA. October 7, 2005.

A New Way to Prevent HIV?
Vaginal microbicides, chemical substances that, when applied to the vagina before heterosexual intercourse, have the potential to prevent or reduce HIV transmission. The non-nucleoside reverse transcriptase inhibitor, TMC120, is one such HIV microbicide candidate currently being tested in Phase I clinical trials. In a recent study, Malcolm, et al measured the daily amounts of TMC120 released from silicone elastomer vaginal rings over a 71-day period. An average TMC120 daily release of 136 µg/day was determined by linear regression. Based on upper limits for the volumes of cervicovaginal fluid and semen, and assuming that the in vivo and in vitro release rates of TMC120 are similar, then the concentrations of TMC120 in the combined fluids are calculated to be within the range required to prevent HIV infection (.01 µM at 10 min, 1.1 µM at 1 hr, 13.2 µM at 12 hr). Study authors concluded that there is the potential for providing protection against HIV infection in the form of a female-controlled vaginal ring device.
Malcolm R, et al. Long-term, controlled release of the HIV microbicide TMC120 from silicone elastomer vaginal rings. Jour Antimicrobial Chemo. 2005; 56(5):954-6.

HIV/HCV Co-infected Liver Transplant Candidates
Liver disease is the leading cause of death for HIV/HCV co-infected patients. Despite equivalent Model for End-Stage Liver Disease (MELD) scores at the time of liver transplantation listing, HIV-infected patients demonstrate significantly shorter pre-transplantation survival time when compared with non-HIV-infected patients. Shorter pre-transplantation survival times among these patients are primarily associated with death related to infection. To improve the survival of the HIV/HCV co-infected liver transplant candidate, Stock recommends early referral of the co-infected patient for liver transplantation. Co-infected patients must meet the same standards as all liver transplant recipients, including a prolonged period of abstinence from alcohol and narcotics, sufficient rehabilitation and demonstration of social support. Additionally, co-infected liver transplant candidates must have CD4-T cell counts greater than 100, the absence of current opportunistic infections and documentation that HIV can be suppressed with an antiretroviral regimen. In the early experience of solid organ transplantation among HIV-infected patients, most transplant centers still determine transplant eligibility according to MELD scores. Unfortunately, by the time liver function deteriorates to a point where the MELD score is sufficiently high for transplant eligibility, HIV-infected candidates no longer meet the entry criteria applied by most transplant centers. Synchronized multi-special care combined with early referral will help to minimize the number of deaths among co-infected patients on liver transplant waiting lists.
Stock G. Rapid deterioration of HIV co-infected patients waiting for liver transplantation is not predicted by MELD. Liver Transplantation. 2005; 11(11):1315-17.

Organ Transplants for HIV Patients
AB228, authored by Assemblyman Paul Koretz and recently signed by California Governor Arnold Schwartzenegger, is the first bill passed by the California State Legislature that prohibits health insurers from denying coverage for organ transplants based solely on a patients' HIV status. Historically, HIV-infected patients have not been considered suitable candidates for organ transplantation due to their relatively shortened lifespan. However, antiretroviral therapy has greatly extended the life expectancy of these patients and studies have shown that organ transplants in qualified HIV-infected patients lead to similar outcomes when compared to non-HIV-infected patients.
California Political Desk. American Chronicle. September 29, 2005. Last accessed October 26, 2005 articleID=2665

Self-Assessment Test for Continuing Medical Education Credit

Brown Medical School designates this educational activity for one hour in category one 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 February 28, 2006. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. The following is not a preferred ART regimen for ART-naïve patients:
   A. Efavirenz plus 3TC
   B. Efavirenz plus TDF
   C. Kaletra® plus TDF
   D. Kaletra® plus 3TC
   E. None of the above

2. The following medications have anti-viral activity against both HIV and HBV:
   A. Tenofovir
   B. 3TC
   C. TDF
   D. A and B
   E. A and C

3. Entecavir has antiviral activity against both HIV and HBV. True or False?
   A. True
   B. False

4. Which of the following mutations is paired correctly with the respective antiviral to which it confers resistance?
   A. D30N; nelfinavir
   B. M184V; FTC
   C. D30N; 3TC
   D. M184V; nelfinavir
   E. A and B
   F. C and D

5. Patients are most likely to transmit HIV during the acute stages of HIV infection. True or False?
   A. True
   B. False

IDCR 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
In the News	5 4 3 2 1	5 4 3 2 1
Save the Dates	5 4 3 2 1	5 4 3 2 1

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

3. What future topics should IDCR address?

4. How can IDCR be made more useful to you?

5. Do you have specific comments on this issue?

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