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## IDCR: Infectious Diseases in Corrections Report, Vol. 8 No. 10

Infectious Diseases in Corrections

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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](http://www.corrdocs.org)).

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#### HEPATITIS C VIRUS (HCV) AND HIV CO-INFECTION IN CORRECTIONS:

#### WHERE DO WE STAND? By Courtney E Colton\*, IDCR \*Nothing to disclose

HCV is one of the most important infections affecting prison populations in the United States (US) and worldwide. Because incarceration is common among previous and current injection drug users, infectious diseases, particularly HCV, are prevalent among the incarcerated population. Additionally, while incarcerated populations are at high risk for HCV and other infectious diseases, many inmates are not routinely screened or treated for HCV infection, despite evidence demonstrating that screening for HCV and other sexually transmitted infections among inmates is feasible, acceptable and efficacious.<sup>1</sup> Because of the high prevalence of HCV within corrections, IDCR has decided to cover HCV in two issues this year. William Cassidy, MD discussed the management of HCV infection in our July 2005 issue. This article will address HIV and HCV co-infection, which affects an estimated 350,000 persons domestically, of which a large proportion are incarcerated in the US correctional system.

Until recently, little data on HIV/HCV co-infection existed. HCV infection is clearly exacerbated in the presence of HIV infection.<sup>4,5</sup> The impact of HCV infection on HIV disease progression is controversial.<sup>2,3</sup> Interactions between HIV and HCV medications, anemia, antiretroviral-induced hepatotoxicity and mitochondrial toxicity are just some of the concerns clinicians must address when treating co-infected patients. Fortunately, however, treatment approaches for both diseases have advanced dramatically over time. Anti-HCV treatment consideration should be given to co-infected patients, particularly because sustained virologic response (SVR) rates upwards of 50% have been documented in co-infected patients with once-weekly pegylated interferon (PEG IFN) and daily ribavirin (RBV), the standard of care treatment for both HCV mono-infection and HIV/HCV co-infection. In the past, the maxim was to initially control HIV infection before initiating HCV therapy. Modern treatment options and clearer under-

standing of the diseases' processes have modified that approach.

#### Epidemiology

Approximately 30% of patients who are infected with HIV are also infected with HCV. While the two viruses share similar modes of transmission, transmission efficiency of each virus differs substantially. HCV is transmitted primarily by percutaneous exposure to blood. In the US, injection drug use is the leading route of transmission. HCV is approximately 10 times more infectious by percutaneous blood exposure to small volumes of blood as compared to HIV. In addition to exposure by injection drug use, HCV may also be transmitted between sexual partners. Because of shared routes of transmission, HCV and HIV co-infection in the United States is common, affecting 85% to 90% of those reporting injection drug use and 10% to 14% among persons reporting high-risk sexual behavior.<sup>4</sup>

Data has demonstrated that HIV infection clearly exacerbates the natural history of HCV infection and accelerates progression to cirrhosis, end-stage liver disease and hepatocellular carcinoma.<sup>5,6</sup> In a recent retrospective cohort study, the survival of 1,037 HCV mono-infected and 180 HIV/HCV co-infected patients after the first hepatic decompensation was analyzed. The survival of co-infected patients was markedly shorter than that of mono-infected patients. Additionally, the 1-, 2- and 5-year survival estimates were 74%, 61% and 44%, respectively, among individuals without HIV co-infection and 54%, 40% and 25%, respectively, among co-infected patients.<sup>7</sup> (Figure 1)

*Continued on page 2*

#### WHAT'S INSIDE

Case Study .....	pg 6
IDCR-o-gram .....	pg 7
HBV 101.....	pg 8
In The News .....	pg 9
Self-Assessment Test .....	pg 10

**HCV/HIV Co-infection... (continued from page 1)**

**Inmate Knowledge of HCV Status**

A large proportion of inmates are unaware of their HCV status. A recent study found that of 121 untested or previously known to be anti-HCV antibody negative inmates in the Australia prison system, 25 were found to be HCV-positive. More than one-half of those who tested positive perceived that they did not have HCV infection, while 44% were unsure of their status. Those inmates who were incorrect about their HCV status were less educated and more likely to have previously been incarcerated.<sup>8</sup>

**Predicting Response to Treatment**

A number of viral and host factors influence treatment response to interferon (IFN)-based therapy in HCV mono-infected patients, including HCV genotype, high viral load, low CD4 T-cell counts, alcohol use, racial distribution and hepatic steatosis. Evidence is beginning to emerge indicating that many of these response factors, particularly genotype and high viral load, may be generalized to co-infection.<sup>17</sup>

HCV genotype has been recognized as one of the strongest predictors of achieving a SVR. Patients infected with HCV genotype 1 are significantly less likely to achieve a SVR, despite longer duration and higher doses of treatment, than patients infected with HCV genotypes 2 or 3.<sup>15,17</sup> This is elaborated upon below in the section entitled "Pegylated Interferon and Ribavirin - The Data".

High viral load negatively impacts response to HCV treatment, as does low CD4 T cell count. A reduced likelihood of achieving a SVR has been documented in patients with HCV viral loads greater than 10<sup>7</sup> copies/mL and HIV CD4 counts less than 500 cells/mL.<sup>9</sup> In one study that evaluated PEG IFN alfa-2a and RBV in HCV mono-infected patients, persons with genotype 1 and a high HCV viral load (>2 x 10<sup>6</sup> copies/ml) had an SVR of 41%, whereas the SVR rate among those with genotype 1 and a low viral load who were treated with the same regimen was 56%. Among persons infected with HCV genotypes 2 and 3 and a high viral load, the SVR rate was 74%, while those with genotypes 2 and 3 and a low viral load who were treated with the same regimen had a SVR of 81%.<sup>10</sup> Similar evidence has shown that co-infected patients with a high pre-treatment HIV viral load are also less likely to achieve a SVR as compared to patients with a low pre-treatment HIV viral load.<sup>17</sup>

Patients who achieve an early virologic response (EVR), defined as an undetectable HCV RNA level or a decrease of 2 log or more

**Figure 1: Probability of Patient Survival by HIV Serostatus**

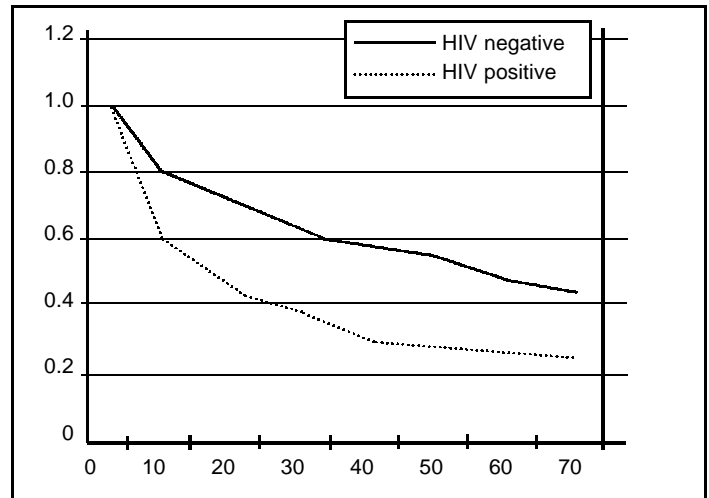


Figure adapted from Pineda J, et al.

in HCV RNA level by week 12, are more likely to achieve a SVR. In the APRICOT study, of patients who had an EVR by week 12, 30% of those in the group given IFN alfa-2a plus RBV, 37% of those in the group given PEG IFN alfa-2a plus placebo and 56% of those in the group given PEG IFN alfa-2a plus RBV, achieved SVRs at week 72. Patients who did not achieve an EVR at week 12 were highly unlikely to have a SVR at week 72 (Figure 2).<sup>17</sup> Other studies have demonstrated similar results.<sup>11</sup>

Several studies among HCV mono-infected persons have been conducted demonstrating that SVR rates are markedly decreased for African Americans compared to Caucasians.<sup>12,13,14</sup> Given the high proportion of African Americans in correctional settings and data demonstrating reduced response rates, the correctional setting provides a unique opportunity to test and treat HCV in this population. Studies assessing the rate of SVR to PEG IFN alfa-2a plus RBV among HIV/HCV co-infected African American patients compared to Caucasian patients have not been done. Additionally, while the basis for lower response rates among HCV mono-infected African Americans is not fully understood, it is recommended that all patients with chronic HCV, regardless of ethnic or racial background, receive anti-HCV therapy.<sup>15,16</sup>

**Pegylated Interferon and Ribavirin - The Data**

SVR rates are lower among HIV/HCV co-infected patients compared to HCV mono-infected patients. However, the three trials

*Continued on page 3*

**Figure 2: Early Virologic Response as a Predictor of Sustained Virologic Response**

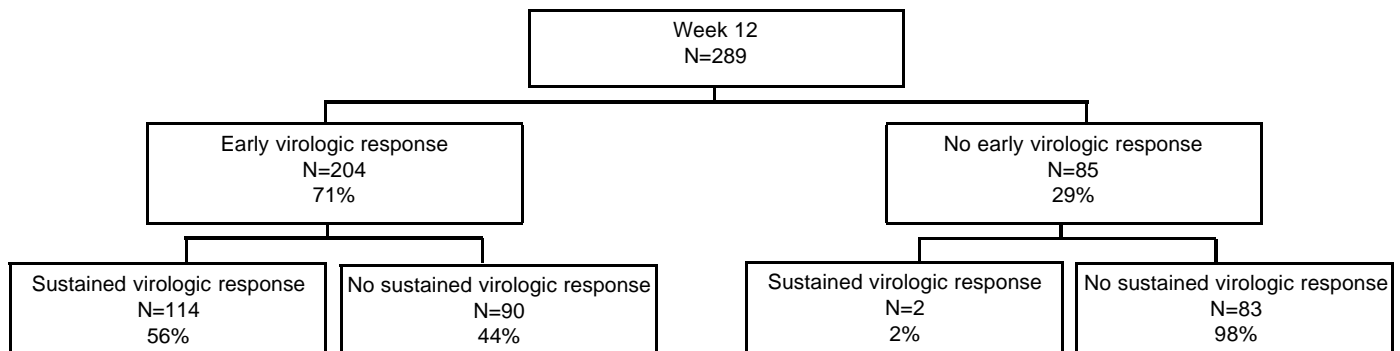


Figure adapted from Torriani, et al.

### HCV/HIV Co-INFECTION... (continued from page 2)

described below have demonstrated that SVR rates approximating 40% among co-infected patients may be achieved with PEG IFN plus RBV treatment - the standard of care for HIV/HCV co-infection treatment - and an even greater percentage of patients achieve histologic improvement with this therapy, warranting treatment of these patients.<sup>15,17</sup>

#### ACTG

In the AIDS Clinical Trials Group (ACTG) A5071 study, 133 co-infected patients were randomized to receive standard IFN plus RBV or PEG IFN alfa-2a plus RBV, achieving SVR rates of 12% and 27%, respectively. Among patients receiving PEG IFN alfa-2a plus RBV, mean SVR rates differed significantly: HCV genotype 1-infected patients achieved a mean SVR rate of 14%, while HCV genotype non-1-infected patients achieved a SVR rate of 73%. Both regimens were well tolerated and neither was associated with loss of HIV disease control. Premature discontinuation rates were similar and low in both groups.

#### RIBAVIC

In a similar, larger European study, the Randomized Controlled Trial of Pegylated-Interferon alfa-2b plus Ribavirin vs Interferon alfa-2b plus Ribavirin for the Initial Treatment of Chronic Hepatitis C in HIV-co-infected patients (ANRS HC02-RIBAVIC), 416 co-infected patients were randomized to receive standard IFN plus RBV or PEG IFN plus RBV, achieving SVR rates similar to those reported in the ACTG trial. Discontinuation rates for this trial were high, with 42% of patients discontinuing therapy early. Episodes of symptomatic hyperlactatemia and pancreatitis occurred in 31% of patients.<sup>18</sup>

#### APRICOT

The largest study to date, the AIDS Pegasys® Ribavirin International CO-Infection Trial (APRICOT), evaluated the efficacy and safety of PEG IFN alfa-2a plus RBV in 868 HIV/HCV co-infected patients. Patients were randomized to one of three 48-week treatment regimens:

- ♦ Group 1: IFN alfa-2a 3 MIU TIW plus RBV 800 mg daily;
- ♦ Group 2: PEG IFN alfa-2a 180 mcg QW plus placebo; or
- ♦ Group 3: PEG IFN alfa-2a 180 mcg QW plus RBV 800 mg daily.

Among patients in this trial, 61% were HCV genotype-1 infected; 15% were cirrhotic. Eighty-five percent of patients were receiving HAART and the mean CD4 T cell count prior to therapy was 530 cells/mm<sup>3</sup>. Overall, mean SVR rates were as follows:

- ♦ Group 1: IFN alfa-2a 3 MIU TIW plus RBV 800 mg daily → 12%;
- ♦ Group 2: PEG IFN alfa-2a 180 mcg QW plus placebo → 20%;
- ♦ Group 3: PEG IFN alfa-2a 180 mcg QW plus RBV 800 mg daily → 40%.

Additionally, HCV genotype 2- and 3-infected patients randomized to group 3 achieved a mean SVR rate of 62%. The overall SVR of 40% among group 3 patients was the highest in any reported study of co-infected patients thus far. (See Table 1 for SVR rates of the three different treatment regimens.)<sup>19</sup>

#### Treatment

HCV treatment is feasible and effective within corrections. A retrospective study of 80 inmates who had received anti-HCV treatment found that adherence to therapy was high. Nearly 80% of

**Table 1: SVR Rates Obtained in APRICOT Study**

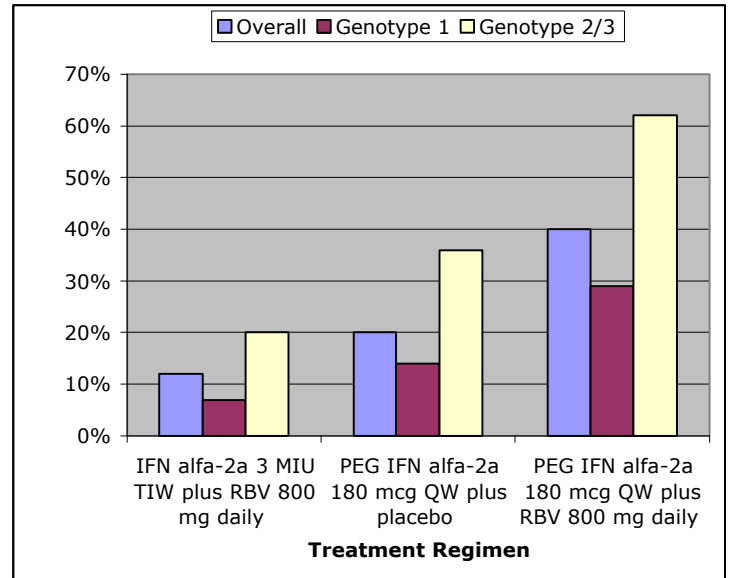


Figure adapted from Pineda J, et al.

inmates completed treatment; 66.3% achieved a SVR.<sup>20</sup> A similar study of 90 male inmates who had received anti-HCV treatment found that adherence to therapy approximated 80%; overall SVR was 55.9%. Furthermore, SVR rates for HCV genotype 1-, 2- and 3-infected persons were 31.6%, 100% and 71.4%, respectively.<sup>21</sup>

The American Association for the Study of Liver Disease (AASLD) recommendations for the management of HCV in HIV-infected persons include the following:<sup>22</sup>

- ♦ Anti-HCV testing should be performed in all HIV-infected persons;
- ♦ HCV RNA testing should be performed to confirm HCV infection in HIV-infected persons who are positive for anti-HCV, as well as those who are negative and have evidence of unexplained liver disease;
- ♦ HCV should be treated in the co-infected person in whom the likelihood of serious liver disease and a treatment response are judged to outweigh the risk of morbidity from the adverse effects of therapy;
- ♦ Initial treatment of HCV in most HIV-infected persons is PEG IFN plus RBV for 48 weeks;
- ♦ Given the high likelihood of adverse events, HIV/HCV co-infected persons on HCV treatment should be monitored closely;
- ♦ RBV should be used with caution in persons with limited myeloid reserves and in those taking zidovudine (ZDV) and stavudine (d4T). When possible, patients receiving didanosine (ddl) should be switched to an equivalent antiretroviral before beginning therapy with RBV;
- ♦ HIV-infected patients with decompensated liver disease may be candidates for orthotopic liver transplantation.

Currently, the only Food and Drug Administration (FDA)-approved treatment for co-infected patients who have compensated liver disease and have not previously been treated with IFN alfa plus RBV (Copegus®, Hoffman-La Roche), both of which were approved for HCV therapy in co-infected patients in February

Continued on page 4

**HCV/HIV Co-INFECTION... (continued from page 3)**

2005.<sup>23</sup> Pegasys® is dosed at 180mcg as a subcutaneous injection given once weekly. Copegus® is available as a 200mg tablet and is administered orally twice daily as a split dose. The most common adverse events reported for this combination therapy include fatigue, headache, pyrexia, myalgia, anxiety, insomnia, alopecia, neutropenia and nausea. Pegasys® is contraindicated in patients who have hepatic decompensation (Child-Pugh score greater than 6.) Copegus® is contraindicated in women who are pregnant. Women of childbearing potential should have a pregnancy test before initiation of therapy with Copegus®.<sup>24,25</sup>

Optimal treatment duration and dosing of both PEG IFN and RBV may need to be adjusted on a case-by-case basis. In contrast to HCV genotype 2- and 3-mono-infected patients who are treated adequately with PEG IFN alfa-2a plus RBV 800 mg/day for 24 weeks<sup>26</sup>, HIV/HCV genotype 2- and 3-co-infected patients should be treated with PEG IFN alfa-2a 180mcg plus RBV 800-1,200mg day for 48 weeks.<sup>27</sup> Both HCV genotype 1 mono-infected patients and HIV/HCV genotype 1 co-infected patients benefit from 48 weeks of treatment with PEG IFN alfa-2a 180 mcg plus RBV 1,000-1,200 mg/day.<sup>22,23</sup>

There are several safety concerns that must be considered when treating the co-infected patient. RBV-associated anemia may be of greater concern in co-infected patients than in HIV mono-infected patients because of the high prevalence of pre-existing anemia. Clinicians should monitor for anemia. Treatment of patients who become anemic during PEG IFN/RBV therapy with erythropoietin alfa may represent an alternative to RBV dose reduction or discontinuation, both of which lower treatment efficacy.<sup>28</sup> Strategies aimed at optimizing doses and adherence to RBV might help to improve responses to HCV therapy in co-infected patients.<sup>29</sup>

The risk of hepatotoxicity associated with different HAART regimens in co-infected patients has not been well elucidated. The risk of HAART-induced hepatotoxicity is greater in co-infected patients than in mono-infected patients, but controversy exists regarding what factors influence this phenomenon. The nucleoside reverse transcriptase inhibitor (NRTI), ddI, is contraindicated in patients

receiving anti-HCV therapy due to an increased risk of hepatotoxicity, lactatemia, pancreatitis and mitochondrial toxicity.<sup>30</sup> Additionally, the non-nucleoside reverse transcriptase inhibitor (NNRTI), nevirapine (NVP), and the protease inhibitor (PI), ritonavir (RTV), may increase the risk of transaminase elevation in co-infected patients.<sup>31</sup> Frequency of laboratory monitoring should be increased in persons with risk factors for hepatotoxicity, especially in those with pre-existing liver disease.

Concern regarding the concomitant administration of PEG IFN, RBV and anti-HIV medications exists. There is increasing concern that d4T may be linked with steatosis in patients receiving anti-HCV therapy.<sup>32</sup> Anemia is a frequently seen side effect of RBV. AZT in combination with RBV has a synergistic effect on anemia, warranting careful monitoring of patients receiving these two medications in combination. Lastly, abacavir (ABC) dosage may need to be reduced in cirrhotic patients.

**Conclusion**

HIV/HCV co-infection among injection drug users is prevalent. Because of the synergism between injection drug use and incarceration, all inmates should be screened, and when appropriate, treated, for HIV and HCV infections. The Infectious Diseases Society of America (IDSA) and the AASLD guidelines for the management of HCV recommend that patients co-infected with HIV and HCV undergo medical evaluation for HCV-related liver disease and consideration for HCV treatment and, if indicated, liver transplantation. The same standard of care should apply to incarcerated populations. Because of the accelerated disease course HCV takes in the presence of HIV, treatment of HCV in co-infected persons is critical. Indeed, it may take priority over HIV treatment. Individualizing the patients' treatment regimen is essential and depends on many factors including medical and psychiatric co-morbidities, liver status, antiretroviral therapy, possible effects of reconstitution of the immune system and length of incarceration, in determining which entity to treat first or in selecting simultaneous treatment. Nonetheless, recently completed randomized controlled trials provide evidence of the safety, tolerability and efficacy of HCV treatment with PEG IFN-alfa plus RBV in HIV-infected individuals.

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## LETTER FROM THE EDITOR

Dear Colleagues,

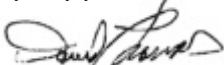
HIV/Hepatitis C virus (HCV) co-infection is commonly seen in the correctional environment. In fact, prisons and jails are probably the greatest single repository of patients co-infected with these viruses. This month's main article focuses on the epidemiology, treatment and control of HIV/HCV co-infection.

The algorithm deals with another aspect of correctional healthcare - control of hepatitis B virus (HBV). One of the most challenging tasks we face during any outbreak is ensuring that all inmates are screened, receive prophylaxis and appropriate follow-up. The February issue of IDCR noted this challenge in a tuberculosis outbreak in a state prison. The problems with hepatitis viruses and corrections are well discussed in a Bureau of Justice Statistics article by Allen Beck and Laura Maruschak<sup>1</sup> as well as two recently published Monthly Morbidity and Mortality Reports (MMWR) on specific HBV outbreaks within correctional facilities.<sup>2,3</sup>

In 2003, Centers for Disease Control and Prevention re-iterated its' 1992 stance that all inmates in all correctional systems should be vaccinated for Hepatitis A Virus (HAV) and HBV.<sup>4</sup> It is most unfortunate that, for economic reasons, many systems do not accomplish this. It is possible that within our lifetime we could eradicate these infectious diseases. The combination of the school-children vaccine program and universal correctional vaccination could lead to the virtual eradication of HAV and HBV.

After reading this issue, you should be familiar with the distinctions between HCV mono-infection and HIV/HCV co-infection and should also be familiar with HBV and HCV treatment options. All of us who work in corrections need to understand our role in the larger public health and advocate for the seamless continuity of care for our patients. Public health and correctional healthcare are determinants of public safety and should be of utmost importance to us all.

Very truly yours,



David Thomas\*, MD

\*Nothing to disclose

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

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## CASE STUDY: Chronic Hepatitis B and D in a Patient Co-infected with HIV

By Bethany Weaver\*, D.O., M.P.H., Acting Instructor of Medicine, University of Washington Center for AIDS & STD Research

\*Nothing to disclose

**CASE:** A 44 year-old Caucasian inmate presents to intake clinic for clinical evaluation as he begins his three-year sentence. He has a history of asymptomatic HIV infection since 1989 and is taking d4T, 3TC and nevirapine, though he reports he misses doses about once per week and is only taking nevirapine 200 mg po qd as he is concerned about liver toxicity. He has chronic active hepatitis B virus (HBV) and hepatitis D virus (HDV) co-infection since at least 1990 and was treated with interferon (IFN) therapy without response for one year in 1995. He has sex with men and uses crystal methamphetamine intermittently. He denies any alcohol use for the last five years but admits to heavy consumption for 10 years prior to this. He is complaining only of fatigue and occasional nausea/vomiting but denies hematemesis. He has been out of care recently due to drug use and thinks his liver enzymes were higher than usual when his doctor last saw him approximately four months ago. On physical exam, he weighs 140 pounds, blood pressure is 132/91, pulse is 89, temperature is 37 and respirations are 16. He appears thin with some temporal wasting, mild scleral icterus, no oral thrush, no lymphadenopathy, clear chest, normal cardiac exam, abdomen benign with no hepatosplenomegaly or distension/ascites appreciated, extremities without edema and skin normal.

### Q: What tests should you order today?

**A:** HIV-1 quantitative viral load, HBV quantitative viral load, HDV antibody, hepatitis B e antigen (HBeAg), hepatitis A antibody, liver function tests (LFTs), metabolic panel with electrolytes, creatinine, CBC and RPR would all be relevant and important tests to consider given this inmates' history and physical exam findings suggestive of possible early cirrhosis with scleral icterus. He also needs a serum alpha-fetoprotein (AFP) level and abdominal ultrasound to screen for cirrhosis and hepatocellular carcinoma (HCC).

His tests show a detectable HIV-1 viral load of 1,000 copies/mL, CD4 count 336 (40%), HBV viral load of 220,000 copies/mL, positive hepatitis D antibody and hepatitis B e antigen, negative hepatitis A antibody, abnormal LFTs with an AST of 90, ALT of 97, total bilirubin 1.9, albumin 3.3, BUN 9, creatinine 0.5, sodium 134 and other electrolytes normal, WBC 4.8, H/H 15/44, platelet count 64k and non-reactive RPR. AFP level is elevated at 27.8 ng/ml with ultrasound showing (1) nodular and coarsened liver consistent with cirrhosis, and (2) evidence of portal hypertension including marked splenomegaly and gallbladder wall thickening.

Based on these findings, you conclude the inmate has chronic persistent HBV and HDV with cirrhosis secondary to this. Though his ultrasound does not show evidence of HCC, he remains at high risk for this and should be rescreened with ultrasound and AFP at regular intervals (ie - every six-12 months). Chronic HBV carriers who are both hepatitis B surface and e antigen positive are at highest risk for HCC (at least 100 times higher than that for non-carriers). You also offer him the HAV vaccine since he is not immune and is at high risk for acquisition with potential for worsening liver disease.

### Q: Are his current medications adequate? If not, what medication changes should be considered and why?

**A:** His HIV and hepatitis medications do not appear to be controlling his infections due to detectable viral loads and evidence of advanced liver disease, though he admits to non-compliance. He should be continued on his current medications until you are able to get an HIV genotype resistance assay. There are several issues to consider in this co-infected patient. Even if his HIV is resistant to 3TC, withdrawal of it might precipitate worsening liver disease. D4T and nevirapine may be contributing to his liver disease/elevated enzymes and should be changed to a different antiretroviral with activity against HBV. In general, avoidance of DDI, d4T (the so-called "D drugs"), nevirapine and some of the protease

inhibitors, such as ritonavir, in co-infected patients is prudent due to risk of liver toxicity. Other options to treat the HBV and HIV infections may be tenofovir, though this is not yet FDA-approved for the treatment of HBV, entecavir, which has been shown to be more active against HBV than adefovir, (recently approved by the Food and Drug Administration in March, 2005) or adefovir. Truvada® and Emtriva® are two co-formulations that also have activity against HBV and reduce pill burden by one. Combination therapy with 3TC and another anti-HBV agent, such as entecavir, should decrease his HBV viral load and reduce liver inflammation. Combination therapy may reduce risk of HBV resistance, though there is not much data to support this yet. Finding a regimen that has activity against HIV and HBV is optimal for the patient to reduce pill burden. However, only adefovir is FDA-approved for use in both HIV and chronic HBV, but is associated with significant nephrotoxicity if given in higher doses necessary to treat HIV. Another course of IFN therapy will not be of benefit to him since he already failed a year of therapy with progression of disease post-therapy.

HIV genotype is sent and shows no resistant mutations. Due to the high HBV viral load and risk of liver toxicity from d4T and nevirapine, you switch him to tenofovir, 3TC and Sustiva®. His HBV and HIV viral load, T cell count, LFTs and HBeAg should be monitored on therapy (ie - every three months).

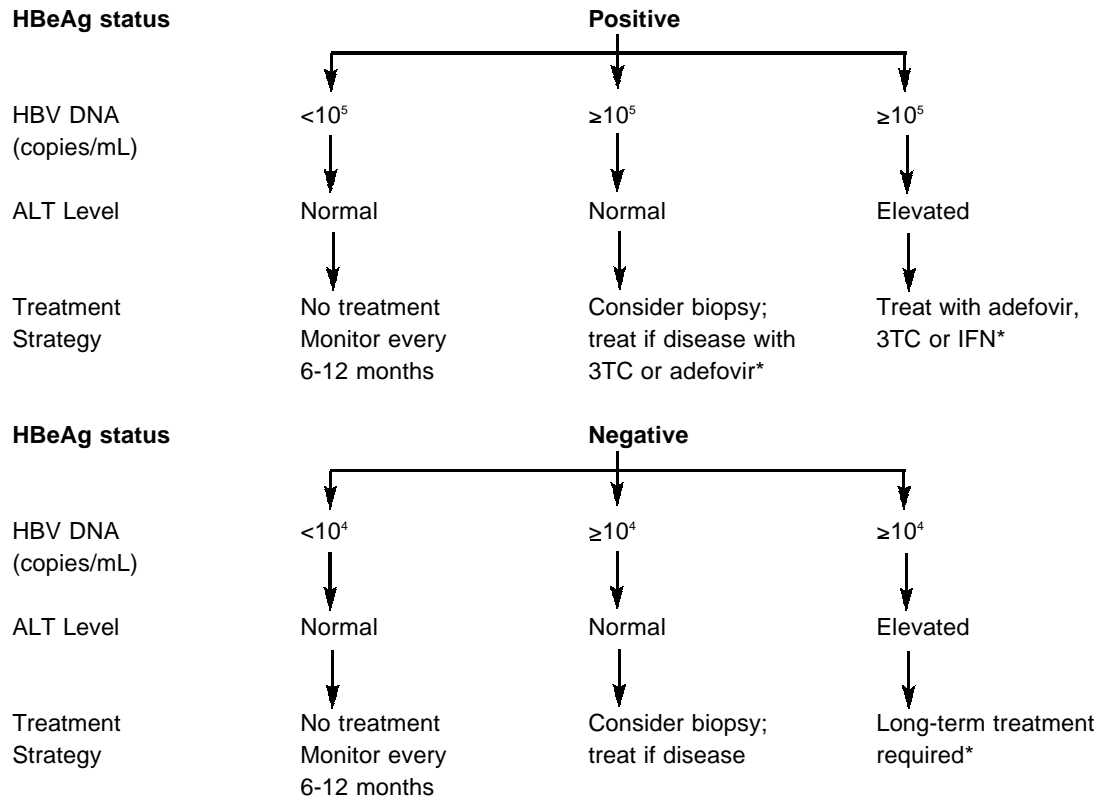
### Discussion

The primary goals of therapy for chronic HBV infection are to reduce viral load burden and treat hepatic dysfunction in an effort to prevent cirrhosis and HCC. There are clear indications for therapy in HBeAg-positive patients since they are at highest risk for early progression to chronic active hepatitis, cirrhosis and HCC. After treatment is initiated, markers of success include improvement in liver function, reduction in viral load, loss of HBeAg and seroconversion to anti-HBe antibodies. Loss of HBsAg and disappearance of viremia occur infrequently (1 to 5% of patients).

In 2004, recommendations from a consensus conference on HIV and chronic hepatitis due to HBV and HCV were published. In the report, the expert panel summarizes several important recommendations, based on findings from the literature: (1) HIV infection enhances viral replication in patients co-infected with HBV. HBeAg-positive chronic HBV is more common in those with HIV and liver disease may be more severe with more rapid progression

(continued on page 7)

## IDCR-O-GRAM: Treatment of Chronic Hepatitis B Virus



**HBeAg-Positive Patients:** Patients should be treated after HBeAg seroconversion until HBV DNA levels are undetectable. Treatment then should be continued for an additional six months. In patients who have HBeAg seroconversion, but in whom HBV DNA levels remain detectable, treatment should continue for six months. Seroconversion should be documented again, then treatment discontinuation should be considered. Patients who relapse can be re-treated. Adefovir should be considered for long-term use in patients who were initially treated with 3TC because of a decreased risk of resistance development.

**HBeAg-Negative Patients:** HBeAg-negative patients tend to have lower serum HBV DNA levels than HBeAg-positive patients, but may still have disease. Recommendations are similar to those for HBeAg-positive patients.

\*Entecavir, though not yet in the guidelines developed by Keefe E, et al, will likely appear in the next revision of guidelines. Entecavir has the best resistance profile when compared to other anti-HBV medications.

Adapted from Keefe E, et al. *Clin Gastroenterol Hepa.* 2004; 2:87-106.

### CASE STUDY... (continued from page 6)

to cirrhosis (BII recommendation); (2) Patients with HIV/chronic HBV, as opposed to HIV alone, are more prone to develop elevated LFTs after initiating antiretroviral therapy (BIII recommendation); (3) Chronic HBV may accelerate HIV disease progression in patients co-infected with both infections (CII recommendation); (4) Treatment should be considered in all patients with HIV/chronic HBV with HBsAg-positivity, detectable HBV DNA and elevated LFTs. For patients who are on or who need treatment for HIV, 3TC, tenofovir or both should be considered as first choice. IFN may be considered for those patients who do not need HIV treatment yet but require HBV treatment (BII recommendation); (5) All HIV-infected patients with end-stage liver disease should be considered as candidates for liver transplantation as long as they do not have advanced HIV disease and have abstained from alcohol and illegal drugs for at least six months (BII recommendation).

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# HBV 101: Recommended Post-Exposure Prophylaxis for Exposure to Hepatitis B Virus

Vaccination and antibody response status of exposed workers*	Treatment		
	Source HBsAg <sup>†</sup> positive	Source HBsAg <sup>†</sup> negative	Source unknown or not available for testing
<b>Unvaccinated</b>	HBIG <sup>§</sup> x 1 and initiate HB vaccine series	Initiate HB vaccine series <sup>^</sup>	Initiate HB vaccine series
<b>Previously vaccinated</b>			
Known responder**	No treatment	No treatment	No treatment
Known Nonresponder <sup>††</sup>	HBIG x 1 and initiate revaccination or HBIG x 2 <sup>^^</sup>	No treatment	If known high risk source, treat as if source were HBsAg positive
Antibody response unknown	Test exposed person for anti-HBs <sup>§§</sup> 1. If adequate, no treatment is necessary 2. If inadequate, administer HBIG x 1 and vaccine booster	No treatment	Text exposed person for anti-HBs 1. If adequate, no treatment is necessary 2. If inadequate, administer vaccine booster and recheck titer in 1-2 months

\*Persons who have previously been infected with HBV are immune to re-infection and do not require post-exposure prophylaxis

<sup>†</sup>Hepatitis B surface antigen

<sup>§</sup>Hepatitis B immune globulin; dose is 0.06mL/kg intramuscularly

<sup>^</sup>Hepatitis B vaccine

\*\*A responder is a person with adequate levels of serum antibody to HBsAg (i.e., anti-HBs > 10 mIU/mL)

<sup>††</sup>A nonresponder is a person with inadequate response to vaccination (i.e., serum anti-HBs < 10 mIU/mL)

<sup>^^</sup>The option of giving one dose of HBIG and re-initiating the vaccine series is preferred for non-responders who have not completed a second 3-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

<sup>§§</sup>Antibody to HBsAg

**Editors Note:** Correctional healthcare workers SHOULD ALWAYS be vaccinated against HBV.<sup>1</sup>

High-risk groups for whom vaccination is recommended include:

1. Persons with occupational risk. HBV infection is an occupational hazard for health care workers and for public-safety workers who have exposure to blood in the workplace. The risk of acquiring HBV infections from occupational exposures depends on the frequency of percutaneous and permucosal exposure to blood or blood-contaminated body fluids. Any health care or public safety worker may be at risk for HBV exposure, depending on the tasks he or she performs. Workers who perform tasks involving contact with blood or blood-contaminated body fluid should be vaccinated. For public safety workers whose exposure to blood is infrequent, timely post-exposure prophylaxis should be considered rather than routine pre-exposure vaccination.<sup>2</sup>

Adapted from CDC. *MMWR*. 2001; 50(RR11):1-42.

## HBV101: Hepatitis B Definitions

Name (Abbreviation)	Definition
Hepatitis B Surface Antigen (HBsAg)	Serologic marker on the surface of HBV. It can be detected in high levels in serum during acute or chronic infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection.
Hepatitis B Surface Antibody (Anti-HBs)	The presence of anti-HBs is generally interpreted as indicative of recovery and immunity from HBV infection. Anti-HBs also develops in a person who has been successfully vaccinated against HBV.
Total Hepatitis B Core Antibody (Anti-HBc)	Appears at the onset of symptoms in acute hepatitis B virus and persists for life. The presence of anti-HBc indicates previously or ongoing HBV infection.
IgM Antibody to Hepatitis B Core Antigen (IgM anti-HBc)	This antibody appears during acute or recent HBV infection and is present for approximately six months.

Table adapted from CDC. *Viral Hepatitis B*. Last accessed September 27, 2005 from <http://www.cdc.gov/ncidod/diseases/hepatitis/b/Bserology.htm>

## SAVE THE DATES

### "Drug-drug Interactions and Metabolic Complications of HIV"

Satellite Broadcast  
October 26, 2005  
12:30-2:30pm EST  
Visit: [www.amc.edu/patient/hiv/hivconf/index.htm](http://www.amc.edu/patient/hiv/hivconf/index.htm)

### 8th Annual Symposium of Controversies in the Management of the HIV-Infected Patient

New York City, NY  
November 4, 2005  
Call: 212.746.4177

### 2005 International Drug Policy Reform Conference

Long Beach, CA  
November 10-12, 2005  
Visit: [www.drugpolicy.org/events/dpa2005/](http://www.drugpolicy.org/events/dpa2005/)

### New England Regional Conference on HIV Treatment & Prevention

November 11, 2005  
Visit: [www.searchforacure.org](http://www.searchforacure.org)

### American Association for the Study of Liver Diseases Meeting

November 11-15, 2005  
San Francisco, CA  
Visit: [www.aasld.org](http://www.aasld.org)

### Update in the Care of HIV Infection

November 30, 2005  
Pittsburgh, PA  
Call: 412.359.4952

### National Viral Hepatitis Prevention Conference

December 5-9  
Washington, DC  
Visit: [www.signup4.net/Public/ap.aspx?EID=2004101E](http://www.signup4.net/Public/ap.aspx?EID=2004101E)

### APHA Meeting and Exposition

December 10-14, 2005  
Philadelphia, PA  
Visit: [www.apha.org](http://www.apha.org)

### Updates in Correctional Health Care

April 8-11, 2005  
Las Vegas, NV  
Visit: [www.ncchc.org](http://www.ncchc.org)

### XVI International AIDS Conference

August 13-18, 2006  
Toronto, Canada  
Visit: [www.aids2006.org](http://www.aids2006.org)

## NEWS AND LITERATURE REVIEWS

### 2nd Annual Stephen Tabet Award Awarded at NCCHC

The second annual Stephen Tabet award was given to Becky Stephenson on October 8, 2005 at the National Conference on Correctional Healthcare in Denver, Colorado. Dr. Stephenson is a tireless advocate for the enhancement of healthcare for the incarcerated. She is a dedicated clinician, is universally loved by her staff and her patients and leads a highly successful HIV program. All of us at IDCR believe that Dr. Tabet would be proud of this wonderful clinician being recognized as the second recipient of this award.

### New HIV Drug Effective, Needs Evaluation

The emergence of drug-resistant HIV-1 mutants often results in treatment failure. Baba, et al recently conducted a study to examine the anti-HIV-1 activity and resistance profile of 2'-3'-didehydro-3'-deoxy-4'-ethynylthymidine (4'-Ed4T), a nucleoside analog that is structurally similar to d4T. When 4'-Ed4T, d4T and 3TC were examined for their inhibitory effects on HIV-1 replication, 4'-Ed4T was found to be the most active among the three compounds; 4'-Ed4T was approximately four times more potent than d4T. Additionally, the anti-HIV-1 activity of 4'-Ed4T was not affected by the K65R mutation and the multi-drug-resistant mutation Q151M complex. The authors concluded that 4'-Ed4T is a potent and selective inhibitor of HIV-1 replication and is less cytotoxic to host cells than d4T in vitro. 4'-Ed4T also shows a unique resistance drug profile that differs from that of known NRTIs, warranting further evaluation of its potential as an anti-HIV-1 agent.

*Baba M, et al. Antimicrobial Agents and Chemotherapy. 2005; 49(8):3355-60.*

### Is HBV Genotype a Predictor of Treatment Response?

Erhardt, et al retrospectively analyzed 165 HBV-infected patients to determine if genotype is a predictor of treatment response. Of patients investigated, 47.3% and 40.0% were HBV genotype A- and D-infected, respectively. Patients infected with HBV genotypes C, B, E and G comprised a small percentage of total

patients analyzed. Overall sustained virologic response (SVR) rate to IFN therapy six months post-treatment was 35%. SVR rates differed dramatically between HBV genotype A and D. Of HBV genotype A- and D-infected patients, 49% and 26%, respectively, achieved a SVR at six months post-treatment. Furthermore, SVR rates at 12 months post-treatment were 47% for HBV genotype A-infected patients compared with 23% for HBV genotype D-infected patients. Erhardt, et al concluded that response to IFN therapy is HBV genotype dependent.

*Erhardt A, et al. Gut. 2005; 54:1009-13.*

### Effective Treatment for Chronic HBV

A recent study sought to determine the efficacy of PEG IFN alfa-2a plus lamivudine (3TC), PEG IFN alfa-2a without 3TC and 3TC monotherapy for the treatment of hepatitis B e antigen (HBeAg)-positive chronic HBV. Eight hundred fourteen patients with HBeAg-positive chronic HBV received either 180ug PEG IFN alfa-2a once weekly plus 100mg oral 3TC daily, 180ug PEG IFN alfa-2a monotherapy once weekly, or 3TC monotherapy, for 48 weeks. All patients were followed for an additional 24 weeks, for a total of 72 weeks. At the end of treatment (week 48), HBeAg seroconversion occurred in 24%, 27% and 20% of patients receiving PEG IFN alfa-2a plus 3TC, PEG IFN alfa-2a monotherapy and 3TC monotherapy, respectively. At the end of follow-up (week 72), HBeAg seroconversion remained highest among patients treated with PEG IFN alfa-2a monotherapy. Virologic response at week 48 was greatest among patients receiving combination therapy. At week 72, suppression of HBV DNA levels to less than 100,000 copies/ml occurred in 32%, 34% and 22% of patients receiving PEG IFN alfa-2a plus 3TC, PEG IFN alfa-2a monotherapy and 3TC monotherapy, respectively. Study authors concluded that in patients with HBeAg-positive chronic HBV, PEG IFN alfa-2a is more efficacious than 3TC.

*Lau G, et al. New Eng J Med. 2005; 352:2682-95.*

## RESOURCES

### Hepatitis B Information

[http://www.hivandhepatitis.com/hep\\_b.html](http://www.hivandhepatitis.com/hep_b.html)

### HIV/HCV Co-infection Information

<http://www.aidsmaps.com/en/news/9E83F736-6D3A-4789-BD09-08960CEDC664.asp>

### CDC. Hepatitis in Corrections information

[http://www.cdc.gov/nchstp/od/ccwvg/ID\\_Hepatitis.htm](http://www.cdc.gov/nchstp/od/ccwvg/ID_Hepatitis.htm)

### CDC. Prevention and control of infections with hepatitis viruses in correctional settings

MMWR. 2003; 52(RR-1):1-44.

### The Hepatitis B Foundation

[www.hepb.org](http://www.hepb.org)

## 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 March 31, 2006. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Approximately what number of persons in the United States are co-infected with HIV and Hepatitis C Virus?
  - a. 250,000
  - b. 500,000
  - c. 750,000
  - d. 1,000,000
  
2. The following factors have been demonstrated to influence treatment response to IFN-based therapy in co-infected patients:
  - a. HCV genotype
  - b. High viral load
  - c. Racial distribution
  - d. a and b
  - e. a, b and c
  - f. None of the above
  
3. HCV genotype-1 infected patients have the greatest likelihood of achieving a SVR with anti-HCV therapy. True or False?
  - a. True
  - b. False
  
4. The following statements regarding HCV treatment in co-infected patients is/are true:
  - a. Treatment duration and dosing of PEG IFN plus RBV should be adjusted on a case-by-case basis.
  - b. There are two FDA-approved treatments for HCV infection in co-infected patients.
  - c. Initial treatment of HCV in most co-infected persons is PEG IFN plus RBV for 24 weeks.
  - d. a and c
  - e. a, b, and c
  - f. None of the above
  
5. Persons who have previously been infected with HBV are not immune to re-infection and hence, require post-exposure prophylaxis upon exposure to HBV. 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
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2. Do you feel that IDCR helps you in your work?

Why or why not?

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