HEPP Report: Infectious Diseases in Corrections, Vol. 5 No. 10

HIV & Hepatitis Education Prison Project

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HEPP REPORT
October 2002 Vol. 5, Issue 10
INFECTION DISASES IN CORRECTIONS

Sponsored by The Brown Medical School Office of Continuing Medical Education.

ABOUT HEPP
HEPP Report, a forum for correctional problem solving, targets correctional administrators and HIV/AIDS and hepatitis care providers including physicians, nurses, outreach workers, and case managers. 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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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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HEALTH STATUS REPORT: INFECTIOUS DISEASES IN CORRECTIONS
Karl Brown, M.D.*, Elizabeth Herbert, Managing Editor HEPP Report*

“3% of Americans incarcerated…12 million released from jails and prisons every year…35% of all cases of active tuberculosis identified among current/recent inmates…500,000 individuals with STDs and 500,000 with latent tuberculosis released every year…30% of all Americans with hepatitis C and 12-18% of those with HIV pass through our nation’s jails and prisons every year…”

The above excerpt was part of the findings of the NCCHC/NIJ “Health Status” report released in May 2002. This national, 3-year-long study was the largest and most comprehensive of its kind ever undertaken. With funding from Congress through the National Institute of Justice, and with substantial support from the Centers for Disease Control and Prevention, the National Commission on Correctional Health Care convened expert panels that included the nation’s most respected researchers, practitioners and scholars in the fields of public and correctional health care. The National Institute of Justice delivered the final report to Congress in May 2002 and is now available on the Internet at http://www.ncchc.org/pubs_sbr.html. This article provides highlights of the report and an abbreviated guide to the management of some of the infectious diseases facing incarcerated populations.

HIV/AIDS

The NCCHC/NIJ report estimates that a number of HIV-infected inmates equivalent to 12% to 18% of the total HIV-infected population in the U.S. were released from prisons and jails in 1996 (98,000 to 145,000 inmates) and that 35,000 to 47,000 inmates in 1997 were infected with HIV (estimated rates are higher for releasees than for current inmates due to the rapid turnover and short lengths of stay in jails). Considering that many infected inmates are unaware of their HIV-positive status - and that jail or prison is often the first opportunity for routine health care - this report re-emphasizes the role of the correctional professional in the detection of new cases of HIV.

Diagnose
Acute HIV infection is often mistaken for another disease or for a minor, self-limited illness. Patients most commonly present with the following symptoms:

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>% Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>90</td>
</tr>
<tr>
<td>Fatigue</td>
<td>80 to 90</td>
</tr>
<tr>
<td>Rash</td>
<td>40 to 80</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>40 to 77</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>70</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>50 to 73</td>
</tr>
<tr>
<td>Headache</td>
<td>32 to 70</td>
</tr>
<tr>
<td>Myalgia / Arthralgia</td>
<td>50 to 70</td>
</tr>
<tr>
<td>Nausea, Vomiting, or Diarrhea</td>
<td>30 to 60</td>
</tr>
</tbody>
</table>

Diagnostic tests for HIV are most commonly done using a serum sample, however, oral swabs may also be used with a high degree of sensitivity. Once diagnosed, treatment is available to patients. Antiretroviral drugs can reduce the level of HIV in the body, increase the number of white blood cells, and improve the immune system. Treatment is available for both acute and chronic infection. All health care providers working in correctional settings should be familiar with the signs and symptoms associated with HIV to enhance early diagnosis and treatment.

Educate
Correctional health providers are in a key position to provide three critical components of HIV prevention: education, testing, and treatment. HIV testing is available at intake in most prison and jail settings, although many newly incarcerated individuals refuse testing at this juncture. Therefore, HIV testing should be easily accessible by request in correctional facilities, and should also be offered whenever a condition that might suggest coinfection with HIV is detected (thrush, shingles, recurrent bacterial pneumonia, STDs, hepatitis C, etc.). For more information on conditions that might flag co-infection with HIV, see the HEPPigram in the Aug/Sept issue of the HEPP Report (www.hivcorrections.org). Counseling and educational programs, especially peer-led discussions of condom use and safe injection practices, are key components of working with inmates to reduce the risk of acquiring or transmitting HIV once they are released.

WHAT’S INSIDE
Ask the Expert: pg 6
HBV 101: pg 7
Self-Assessment Test: pg 9

Continued on page 2

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**Health Status Report...**

*(continued from page 1)*

ing signs and symptoms: fever, fatigue, lymphadenopathy, pharyngitis, rash, and weight loss (see Table 1). Chronic infection, depending on the stage, may be symptom-free. Symptomatic HIV infection should be treated.

HIV diagnosis is most commonly made with a routine serology assay (ELISA and confirmatory western blot), although several HIV test technologies have recently been approved by the FDA for diagnostic use in the United States. These include rapid blood, urine and oral fluid tests (for a list of approved tests, go to http://www.fda.gov/cber/products/testkits.htm). The FDA is soon expected to approve a fast-response finger-prick HIV blood test, which requires only a drop of blood and produces results in less than an hour. These rapid tests may be particularly useful for jails in relation to occupational exposure to blood from a source of unknown HIV status, and in follow-up testing of those who have been exposed to HIV. During acute seroconversion, the serum ELISA and western blot are usually negative; whereas the quantitative HIV viral load will be positive, and is the diagnostic test of choice. Approximately 60 or more days after the acute infection, seroconversion should occur. All cases of chronic infection will have a positive HIV ELISA and western blot.

**Treat**

Highly Active Antiretroviral Therapy (HAART) is the standard of care for treatment of HIV infection. There are currently 19 approved antiretroviral agents, each of which has potential side effects and drug-drug interactions. Furthermore, HIV treatment recommendations continually evolve. For these reasons, HIV treatment should be overseen by clinicians with special expertise in this disease. A recent listing of HAART doses and side effects and a discussion of the latest antiretroviral drugs can be found in the May 2002 HEPP Report and the November 2001 HEPP Report (www.hivcorrections.org). An update on HIV treatment news from ICAAC and IDSA will be available in the December issue of HEPP. For the latest HIV treatment guidelines, go to http://hivatis.org/trygdins.html#Adult.

**Syphilis**

**Educate**

The NCCHC/NIJ report recommends a strategy of education and screening to prevent and treat highly prevalent infectious diseases such as syphilis, gonorrhea, and chlamydia. Rapid screening tests are highly recommended, as they reduce the time between testing and the start of treatment, increasing the likelihood that infected patients will be treated before being released.

The CDC recently reported the prevalence of syphilis in women in three correctional facilities in the United States to be 35% of women at intake. Figures from the NCCHC/NIJ report are certainly consistent: between 46,000-76,000 inmates were infected with syphilis in 1997. Additionally, the CDC published newly-updated “Sexually Transmitted Diseases Treatment Guidelines” in May 2002, available online at www.cdc.gov/std/treatment/default.htm.

The prevalence of AIDS among inmates is five times higher than among the general U.S. population, according to the Report to Congress.

**Diagnose**

Patients infected with syphilis may present with symptoms of primary syphilis (ulcer or chancre at the infection site), secondary syphilis (skin rash, mucocutaneous lesions and/or lymphadenopathy), or tertiary syphilis (cardiac, ophthalmic, auditory abnormalities, and/or gummatous lesions). The possibility of HIV infection should be considered whenever syphilis or any other STD is diagnosed. Testing for syphilis is performed routinely in most correctional facilities. A preliminary diagnosis is made by non-treponemal tests such as the Venereal Disease Research Laboratory test [VDRL] or Rapid Plasma Reagin [RPR] test. More specific tests (fluorescent treponemal antibody absorbed [FTA-ABS] and T. pallidum particle agglutination [TPPA]) are used to confirm infection. Low titer false-positive nontreponemal test results are very common in the setting of HIV infection.

**Treat**

The preferred drug for treating all stages of syphilis is Penicillin G, administered intramuscularly (IM). For late latent syphilis or latent syphilis of unknown duration, the recommended regimen is benzathine penicillin G, 7.2 million units total, administered as three doses of 2.4 million units IM each at 1-week intervals. Treatment of primary syphilis only requires one dose (2.4 MU IM). Alternative regimens for penicillin-allergic patients can be found at www.cdc.gov/std/treatment/default.htm.

When syphilis must be treated during pregnancy, in a penicillin allergic patient, the recommendation is to desensitize the patient (to penicillin) and then follow the usual penicillin treatment recommendations. This desensitization should take place in a hospital as IgE mediated severe reactions can occasionally occur. Erythromycin is no longer recommended for treatment of pregnant women as it is considered unreliable for cure of the infected fetus.

Presumptive treatment for other STDs is usually carried out in conjunction with treatment for syphilis, since gonorrhea and chlamydia are "fellow-travelers." For all patients, including HIV-infected syphilis patients, careful follow-up of the RPR or VDRL, which should show decline over time, is essential. A decline of two tube dilutions is considered significant and should be seen by three months post-treatment.

**Gonorrhea and Chlamydia**

**Educate**

Gonorrhea (GC) and chlamydia are highly prevalent in correctional populations - the NCCHC/NIJ report estimates that 18,000 inmates were infected with GC, and 43,000 with chlamydia, in 1997. The CDC report in 1998 documented rates in women of 27% and 8% for chlamydia and GC, respectively.

Peer-led educational intervention has been proven to work in many communities, and culturally appropriate messages are most likely to be effective, according to the NCCHC/NIJ report. The connection between concurrent STDs and the increased risk of acquiring or spreading HIV needs to be clearly explained to patients to allow them to make informed decisions to protect their health and the health of those they care about. Both male and female condoms can be effective in decreasing the transmission of GC and chlamydia. Rapid testing methods are cost-effective and can be invaluable in the prompt diagnosis of chlamydia and GC.

**Diagnose**

Symptoms of GC and chlamydia-related urethritis and cervicitis can differ for men and women. Among men, asymptomatic infections are common. For women, GC is usually asymptomatic, but C. trachomatis is often asymptomatic and can remain so for many years. Women can present with mucopurulent cervicitis, characterized by a purulent or mucopurulent endocervical swab specimen. Women can also present with salpingitis or tubo-ovarian abscess. Ligase chain reactions are simple tests than can be performed on urine samples negating the necessity of a pelvic exam in women or a urethral swab in men. These tests are more sensitive than traditional cul-

Continued on page 4
Dear Correctional Colleagues:

If you’ve been watching the news on corrections lately, you’ve seen the news media “spin” on NCCHC/NJ Report to Congress that claims “Tens of thousands of inmates are being released every year with undiagnosed or untreated communicable disease, chronic disease and mental illness.”

If the truth be known, “The Health Status of Soon-to-be-Released Inmates: A Report to Congress” doesn’t contain any surprises. As correctional health providers, we all know that infectious diseases are common in correctional settings. What we really need to know is how to rapidly diagnose the infections, and how to manage them in the correctional setting.

What’s really new about the NCCHC/NJ Report to Congress is that you now have access to the prevalence of the communicable diseases that are described in the report and our accompanying “how to” manual on the management of each of these diseases does not do the report full justice.

Why do these data deserve re-emphasis? Because they clarify the role of the correctional health provider on the front line of infectious disease control. Your role is critically important, not only because you protect your fellow staff and inmates in your institution from communicable disease when you accurately diagnose and treat, but also because in the course of carrying out your duties, you protect individuals in the communities to which these patients return. Our role is to try to provide you with the information and tools you need to carry out your critically important job. After reviewing this article, you should be familiar with infectious diseases that are extremely common in corrections, and should be able to list the methods used to diagnose, treat, and manage these illnesses in correctional settings.

In closing, we want to extend a warm welcome to Beth Herbert, our new Managing Editor. She comes to us with an extensive writing and editing background and website skills to boot! If this month’s issue is any indication (she started working on it less than four weeks ago) we’re in very capable hands. Welcome Beth! As always, please feel free to contact us with any comments or suggestions. We’re also happy to announce that we mark five years of continuous publication with this issue. We’ve enjoyed every aspect of writing, editing and publishing the HEPP Report over the past five years, and look forward to many more years of service to our correctional colleagues.

Sincerely,

Anne S. De Groot, M.D.  Joe Bick, M.D., Co Chief Editors

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Published monthly and distributed by fax, HEPP Report provides up-to-the-minute information on HIV and hepatitis treatment, efficient approaches to administering treatment in the correctional environment, national and international news related to HIV and hepatitis in prisons and jails, and changes in correctional care that impact HIV and hepatitis treatment.

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Health Status Report...  
(continued from page 2)

ture techniques for C. trachomatis and are currently the preferred means of detecting this organism. If diagnostic tools (e.g., Gram stain and/or culture) are unavailable, or if patients are unlikely to return for a follow-up evaluation, those with classic symptoms should be considered for empiric treatment for both GC and chlamydia.

Treat

Patients infected with N. gonorrhoea are often infected with C. trachomatis, leading to a recommendation that patients being treated for gonococcal infection also be treated with a regimen effective against uncomplicated genital C. trachomatis infection. Routine dual therapy without testing for chlamydia can be cost-effective for populations (such as inmates) in which dual infection rates are high (over 10%).

Single-dose regimens should be provided by directly observed therapy (DOT) to ensure adherence. The recommended regimens are ceftriaxone 125 mg IM or cefixime 400 mg po or ciprofloxacin 500 mg po or ofloxacin 400 mg po PLUS azithromycin 1 g orally in a single dose or doxycycline 100 mg orally twice a day for 7 days. These regimens cover both GC and chlamydia.

Tuberculosis

Educate

According to the Report to Congress, eliminating TB depends heavily on those working in correctional health care. Coordinated care and discharge planning to outside health department or health facilities for continuation of care are paramount in completing care. Thus educational efforts are best directed at health care and correctional staff. Intensified screening, treatment, and containment efforts among prisoners are vital components in the CDC’s overall plan to eliminate TB in this country.

Nationwide, the rate of active TB cases in the incarcerated is 10-20 times greater than that in the general U.S. population. An increasing proportion of TB cases in this country are developing among the foreign born. During 2000, a total of 16,377 U.S. cases of TB were reported - 46% of those cases among foreign-born persons. Foreign born individuals often pass through correctional facilities if they are detained by the INS or for other reasons. As with STDs, screening for TB is usually routine at intake in jail and prison settings. In addition, correctional health providers should have a low threshold for repeating TB screening procedures during incarceration, so as to prevent repeats of outbreaks of TB in corrections.  

Diagnose

At intake, all inmates should be interviewed and examined for signs and symptoms consistent with active TB: a productive, prolonged cough (a cough lasting for at least 3 weeks), hemoptysis (coughing up blood), fever, chills, night sweats, easy fatigue, loss of appetite, or weight loss. Those showing symptoms should be masked and placed in negative pressure respiratory isolation until active TB can be ruled out. PPD skin testing should be performed on patients with prior negative or unknown results; follow-up tests for individuals who have a positive PPD skin test may include posterior-anterior chest radiographs, sputum-smear and culture examinations. TB screening by PPD is usually repeated annually in prison settings. New PPD conversions may signal TB transmission within the facility.

TB can be difficult to diagnose in individuals infected with HIV, so all HIV-infected persons, regardless of whether they are symptomatic or have a positive skin test, should also be screened with a chest radiograph.  

Improved communication between corrections and city and state departments of health is a key component of treating and containing infectious diseases in prisons and jails.

Treat

Treatment consists of regimens that include at least four drugs until drug sensitivity is available, isoniazid, rifampin (RIF), pyrazinamide (PZA), and either ethambutol or streptomycin are first-line agents (for more information on managing TB in corrections, see the March 2002 HEPP Report at www.hivcorrections.org or http://hivatis.org/trtgdnls.html#Tuberculosis). Pyrazinamide and streptomycin should not be used to treat pregnant women. TB-infected patients who are HIV-positive and are on a HAART regimen containing a PI or an NNRTI may need to receive rifabutin instead of rifampin, and may also require dose adjustments in their HIV medications. HIV infected patients diagnosed with active tuberculosis should be managed by someone expert in management of dually infected individuals as the treatment may become complicated.  

Since treatment of latent tuberculosis infection (LTBI) can reduce the risk of active TB disease developing by approximately 90%, the CDC and the Institute of Medicine strongly recommend prophylaxis. The recommended course is INH daily or twice weekly for nine months. Short course treatments with RIF and PZA or RIF alone can be used in carefully selected and monitored patients. Treatment of LTBI will protect not only corrections but also the communities to which releases will return.

It is critical that inmates being treated for active TB are on directly observed therapy to ensure adherence to therapy. Inadequate or interrupted treatment can result in relapse, continued transmission, and the development of drug-resistant disease.

Hepatitis A, B, and C

Hepatitis A

Hepatitis A is usually a self-limited illness and rarely requires supportive care. Approximately 33% of adults in the U.S. have evidence of past infection. There is no chronic phase of HAV infection. The most common route of infection is fecal-oral through contaminated food products, and sexual transmission, predominately among men who have sex with men (MSM) and among intravenous drug users. Though usually self-limited, HAV has been associated with severe symptoms, including death, in the elderly (>55 years) and in persons with chronic liver disease. Vaccination is the most effective means of preventing transmission of hepatitis A. Current vaccines include Twinrix (combination vaccine for both hepatitis A and hepatitis B), Havrix, and Vaqta.

Hepatitis B

The NCCHC/NIJ report estimated that more than 36,000 inmates - an estimated 2% of prison and jail inmates and releasees in 1997 - had current or chronic hepatitis B infection. Inmates released from prison who were HBV-positive represented 12% of the total number of cases in the U.S. Vaccination against the hepatitis B virus (HBV), available since 1982, has led to a decline in the prevalence of HBV in the general population. However, 20 to 80% of U.S. inmates have evidence of past or chronic HBV infection, and 0.8 - 1.4% of inmates acquire HBV while in prison. High rates of HBV infection occur in people who have multiple sex partners and share needles (including tattooing), and cellmates of inmates with acute or chronic HBV infection (analogous to household contacts) are also at risk for acquiring HBV. Since HIV and HBV have similar methods of transmission, coinfection is common.

Educate

While avoiding contact with contaminated blood, semen, vaginal fluids, and wound exudates is the only way to be completely protected against HBV infection, immunization is also an effective means of preventing...
HEALTH STATUS REPORT...

(continued from page 4)

infection, particularly among high-risk groups. Therefore, in a forthcoming issue of MMWR, the CDC is expected to recommend that inmates who participate in high-risk behaviors receive HBV vaccine while incarcerated. Recombivax HB and Engerix-B are two HBV vaccines available in the U.S. Needle exchange and clean needle programs are other important interventions that may reduce HBV risk in the community. Simultaneous protection against HBV and HAV can be accomplished with the combination vaccine, Twinrix.

Diagnose

Only 25 - 50% of cases of acute HBV infection are symptomatic; the remainder are asymptomatic or have inconsequential symptoms. After a one-week to six-month incubation period, symptoms include malaise, weakness, anorexia, nausea, vomiting, and right upper quadrant pain. The symptoms abate during the icteric phase (jaundice), lasting for approximately three weeks. The hepatic transaminases peak, and then begin to decline. During the convalescent phase, which may last for up to six months, symptoms completely resolve.

Most persons exposed to HBV have a well-defined immunologic response that results in the resolution of the infection and protective immunity. The first serologic marker of HBV infection to appear is Hepatitis B surface antigen (HBsAg), a protein on the surface of the virus. The antigen usually persists in serum throughout the period of clinical illness, and is commonly used to diagnose acute HBV infection. (Please see the HEPPIPgram for more information on HBV serologies during acute and chronic infection). The presence of anti-HBsAg, also known as HBsAb, indicates resolution of acute disease and development of immunity. Persistent HBsAb suggests the present of chronic infection.

Treat

While there is no specific therapy for acute viral hepatitis (other than supportive therapy), chronic HBV infections can be treated with one of three drugs: Interferon, Lamivudine, or Adefovir. Adefovir (made by Gilead Sciences Inc. and sold as Hepsera) was recently given FDA approval. Tenofovir, approved for use in HIV infection, also has significant anti-HBV activity. Patients with chronic HBV and HIV coinfection are less likely to respond to interferon treatment for chronic HBV infection. When lamivudine is included in an antiretroviral regimen in patients with HIV and HBV coinfection, HBV viral replication is often significantly reduced for the duration of lamivudine treatment.


Hepatitis C

HCV is the most common blood-borne infection in the U.S., with nearly 4.5 million people infected. At least 303,000 - 332,000 prison and jail inmates were infected with hepatitis C in 1997, according to the NCCHC/NIJ report. The 17 to 18.6 % prevalence range of hepatitis C among inmates - which the study states may be an underestimate - is 9 to 10 times higher than the prevalence of HCV in the nation’s population as a whole. HEPP Report (www.hivcorrections.org) recently reviewed the problem of HCV infection in corrections (March 2002) and new guidelines on the treatment of HCV infection (August 2002).

Educate

The HCV test results can be used as an opportunity to educate inmates about the risks for acquiring HCV (if they are HCV negative) and the importance of avoiding alcohol to prevent progression of the disease, if HCV is diagnosed. Education also allows HCV-infected inmates to understand their illness, take better care of themselves, and prevent transmission to others.

Diagnose

All inmates should be evaluated for HCV risk factors; those with HCV risks should be offered testing. Current FDA-approved antibody tests for HCV are highly sensitive and specific (99%), reproducible, and inexpensive.

Treat

Most correctional facilities are in the process of developing protocols for triaging HCV-infected patients for treatment. Important changes in the management of HCV infection are reviewed in the August/Sept issue of the HEPP Report (www.hivcorrections.org). Additional information on treating HCV, including dosing schedules, can be found in the March 2002 HEPP Report. Updated guidelines can be found at http://consensus.nih.gov/cons/116/116cdc_intro.htm. Currently, the best regimen for infected patients appears to be a 24- or 48-week course of the combination of pegylated IFN and ribavirin.

Conclusion

Whereas the NCCHC/NIJ report might seem to suggest that correctional health providers are sending patients home to their communities with infectious diseases, the problem is much more complex. Incarceration concentrates individuals who have had poor access to health care and extensive exposure to communicable diseases. Protocols to address these infections are being developed and many are already in place. Appropriate diagnosis and treatment should be provided, and discharge planning should be included in the overall plan to treat and contain infectious diseases. Improved communication between corrections and state departments of health is necessary. One example of this is illustrated by the New York City Department of Health involvement with correctional facilities in its sphere of influence, local departments of health can provide important assistance to correctional facilities by documenting rates of disease in incarcerated individuals and helping to coordinate the continuation of care and tracking of contacts within their communities. Much work remains to be done, of course, but protocols and procedures can be established to enable correctional providers to excel in their roles at the front line of community health.

Disclosures:

“Nothing to disclose

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A 40 year-old male is incarcerated for an expected two-year term. At the inmate's intake health assessment the nurse practitioner takes note that the patient has chronic hepatitis B virus (HBV) infection (surface antigen-positive [sAg+]). He was tested six years ago when he reported to his primary care doctor with symptoms of acute hepatitis; his liver enzymes were then in the mid 500s. These normalized within six months.

Currently his enzymes are again elevated, with ASTs of 140-164 and ALTs of 111-147. The physical exam shows no obvious indications of chronic HBV and no evidence of cirrhosis. His HBV DNA viral load is 1.2 million copies/ml and he is hepatitis B e-antigen positive (HBeAg). He is HIV-negative and hepatitis C (HCV)-negative. He denies intravenous drug use, but acknowledges occasional use of crystal methamphetamine and having two or three drinks per day with occasional binging (on the outside). He feels that completely stopping drinking is an unrealistic expectation for him once he is released. He is very interested in starting treatment and wants to discuss his options.

**Discussion:**

Q. Is this patient a good candidate for treatment?

A. Yes, this patient is a good candidate for treatment, given the presence of HBeAg, the elevated ALT, and his motivation to be treated. Potential treatment endpoints include HBeAg seroconversion, HBV DNA suppression, liver histologic improvement, and improved clinical outcome. The presence of HBeAg and HBV DNA indicates active viral replication, which appears to be associated with an increased risk of hepatic complications.

A second important factor is the baseline ALT level. For both interferon [3] and lamivudine [4], higher response rates are observed in patients with higher ALT. In a two-year study of lamivudine, HBeAg conversion rates increased with increasing baseline ALT: 7%, 17%, 37%, and 80% for patients with normal, 1-2x normal, 2-5x normal, and >5x normal baseline ALT, respectively [4].

Finally, the ability to adhere to a daily medication schedule must be considered. A major drawback of lamivudine therapy is viral resistance. The emergence of viral resistance occurs at a rate of 15% after one year of therapy, and 65% after five years of therapy [5]. Although no data has been published linking adherence rates to the development of antiviral resistance in hepatitis B therapy, a strong relationship between adherence and the development of HIV drug resistance has been reported and therefore should be anticipated for HBV infection [6]. Furthermore, poor adherence has been linked to drug and alcohol use [7]. Active drug and alcohol use in this patient may increase his likelihood of treatment failure. This patient's incarceration, with the advantage of supervised medication dosing and limited access to alcohol, may improve his likelihood of response to oral therapy.

Q. Would you use lamivudine or adefovir (or even tenofovir), or both?

A. The advantages of alpha interferon therapy for the treatment of chronic hepatitis B should be reviewed. With alpha interferon, the treatment course is only 4 months, viral resistance is rare, and HBeAg seroconversion rates are durable. Although HBeAg conversion rates are low in Asians from endemic areas where vertical transmission is most common - probably because of immune tolerance [8] - response rates in patients from non-endemic areas are approximately 33% (end of treatment responses are approximately 40% but sustained responses only 10% per Lee, et al in NEJM 1997)[9]. Patients treated with interferon experience symptoms including fatigue, depression, myalgias, arthralgias, and hair loss and may also develop laboratory abnormalities such as pancytopenia. However, for those who can tolerate these side effects, interferon may still be the best option for treatment of chronic hepatitis B. Initial treatment with interferon also preserves the availability of lamivudine for use in a pre-transplant setting, when potent suppression of HBV DNA is necessary [10].

Unlike lamivudine, adefovir dipivoxil, recently approved by the FDA, does not appear to be associated with a high rate of HBV resistance. Although data beyond one year is not yet available, no resistance mutations to adefovir dipivoxil were observed among patients treated for chronic hepatitis B. Initial treatment with interferon also preserves the availability of lamivudine for use in a pre-transplant setting, when potent suppression of HBV DNA is necessary [10].

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There are now three FDA-approved treatments for the management of chronic HBV infection: lamivudine, interferon-alfa-2b, and, most recently approved, adefovir dipivoxil. Adefovir dipivoxil is the first nucleotide analogue to receive FDA approval for the treatment of chronic hepatitis B.

### Antiviral Agents for the Treatment of Hepatitis B

**NAME** | **ACTIVITY** | **KEY FINDINGS**
--- | --- | ---
**FDA-Approved Anti-HBV Agents**
Adefovir dipivoxil | Inhibits HIV reverse transcriptase and HBV DNA polymerase | • Used at lower doses than were studied for HIV
• Produced -4.80 log10 copies/mL reduction in HBV DNA (9/35 patients undetectable) at week 72 among lamivudine-resistant patients
• 9% HBeAg seroconversion rate

Lamivudine | Inhibits HIV reverse transcriptase and HBV DNA polymerase | • Monotherapy (100 mg/day) associated with HBV DNA clearance or reduction in nearly all patients
• HBeAg seroconversion in only 17% at 1 year
• YMDD mutants are lamivudine-resistant, but probably replication-impaired
• Lamivudine withdrawal may result in severe hepatic flares

Interferon-alfa-2b | Antiviral and immunomodulatory effects | • Compared with lamivudine, comparable clinical response rates and higher HBeAg seroconversion and HBsAg clearance rates
• Poor results in perinatally acquired disease and among Asian patients
• Superior efficacy and reduced toxicity of pegylated forms of interferon

**Investigational Anti-HBV Agents**
Tenofovir disoproxil fumarate | Inhibits HIV reverse transcriptase (FDA-approved) and HBV DNA polymerase | • Active against HBV at doses used to treat HIV
• Produced -3.94 log10 copies/mL reduction in HBV DNA at 48 weeks among 12 lamivudine-resistant patients
• 1/12 HBeAg seroconversion

Emtricitabine | Inhibits HIV reverse transcriptase and HBV DNA polymerase | • 61% undetectable HBV DNA at 1 year at 200 mg/day, and 50% HBeAg seroconversion

L-dT | Inhibits HBV DNA polymerase only | • Up to 3.6 log10 copies/mL reduction in HBV DNA at 4 weeks among patients with wild-type HBV

**REFERENCES:**


**DISCLOSURES:** Nothing to disclose
**Save the Dates**

40th Annual Infectious Disease Society of America (IDSA) Meeting
October 24-27, 2002
Chicago, Illinois
Call: 703.299.0200
Email: info@idsociety.org
Visit: http://www.idsociety.org/
ME/AM2002/ToC.htm

4th Annual National Corrections Telemedicine Conference
November 24-26, 2002
Tucson, Arizona
Call: 520-626-4785
Email: hatheway@u.arizona.edu

North American AIDS Treatment Action Forum
December 8-11, 2002
New Orleans, Louisiana
Fee: before Nov. 8, $150 members
$175 non-members
After Nov. 8, $225
Call: Paul Woods,
202.483.6622 ext. 343
Email: pwoods@nmac.org
Visit: www.nmac.org/nataf/2002

**Inside News**

**HIV**

Once a Day Dosing Approved for Epivir (lamivudine)
The FDA has approved an expanded label indication for GlaxoSmithKline’s Epivir (lamivudine), to be used once daily to treat HIV infection in combination with other antiretroviral agents. The recommended oral dose of Epivir for adults is 300 mg daily, administered either as 150 mg twice daily or 300 mg once daily.
FDA, 7/2/02, http://hivatis.org/newdose.html

Changes in Agenerase Product Labeling
The product labeling for Agenerase (amprenavir) has been changed to reflect new precautions related to the use of the drug with methadone and with oral (hormonal) contraceptives. The complete Agenerase label can be found at http://www.fda.gov/cder/foi/label/2002/21007s1120103s10lbl.pdf.
FDA, 8/12/02.

**HCV**

FDA Approves Adefovir for Chronic Hepatitis B
The FDA has approved the antiviral agent adefovir dipivoxil for the treatment of chronic Hepatitis B. Adefovir dipivoxil, made by Gilead Sciences Inc. and sold as Hepsera, is the first nucleotide analogue to receive FDA approval to treat chronic HBV. The drug, administered as a 10 mg oral tablet, also proved effective in patients who were resistant to lamivudine.

Trial to Study Hepatitis C in African Americans
NIH has enrolled 400 adult patients - 200 African Americans and 200 white Americans - in a study of viral resistance to antiviral therapy for chronic hepatitis C. All participants will receive a course in the combination of peginterferon alfa-2a and ribavirin. Particular emphasis will be placed on determining why some patients respond more positively to therapy than others. A description of the trial will be available at http://www.edc.gsp.hivatc.pitt.edu/virahepc.

**Effort Made to Inform Inmates of HCV status in NJ Prisons**

New Jersey corrections officials launched a mass notification program to inform HCV-positive inmates of their diagnosis. According to a medical audit, all 1,169 prisoners in the state who are known to have the disease have been informed of their disease status. While most inmates receive their diagnosis within a year of being tested, 121 waited between one and two years to be informed. Twenty-one inmates who tested positive for HCV were recently released from prison without being informed of their diagnosis. Although NJ estimates that 5% of prisoners in the state have hepatitis C, the state does not currently provide treatment for that disease.
Philadelphia Inquirer, 10/6/02

**HCV/HBV and HCV Coinfection**

New Safety Information for Videx (Didanosine, ddl) used with Ribavirin
The Videx (Didanosine, ddl) label has been revised to include new, precautionary information about co-administration of Videx and ribavirin (RBV) in HIV/HCV co-infected patients. The new label includes the warning that "Co-administration of ribavirin with Videx should be undertaken with caution, and patients should be monitored closely for didanosine-related toxicities. Videx should be suspended if signs or symptoms of pancreatitis, symptomatic hyperlactatemia, or lactic acidosis develop."

**ICAAC Report on the use of Tenofovir on HIV- and HBV-infected persons**
At the 42nd ICAAC meeting in San Diego, researchers reported on the use of tenofovir in HIV/HBV co-infected patients. In the test, 18 patients received the standard dose of 300mg of tenofovir once daily as part of their HIV regimen. During the study period, two patients converted lost HIV virological control as a result of the tenofovir administration. The researchers reported on the use of tenofovir in HIV- and HBV-infected persons.
ICAAC Conference Report (all reports archived at http://www.natap.org)

**Resources & Websites**

CDC Recommendations and Guidelines Division of HIV/AIDS Prevention

MEDLINE plus: Hepatitis B

NIH Hepatitis Consensus: Management of Hepatitis C
http://consensus.nih.gov

CDC: Sexually Transmitted Disease Guidelines, 2002
http://www.cdc.gov/std/treatment

CDC Division of Tuberculosis Elimination
http://www.cdc.gov/nchstp/tb/

Canadian HIV/AIDS Policy and Law Review 2002
http://www.aidslaw.ca/Maincontent/otherdocs/Newsletter/3vol5no1022002/issue.htm

Canadian resource on HIV/AIDS and prisons PROS & CONS: A Guide to Creating Successful Community-based HIV/AIDS Programs for Prisoners By Rick Lines
To obtain a free copy (plus postage) call 877.999.7740, email aidsida@cpha.ca, or go to www.clearinghouse.cpha.ca
Self-Assessment Test for Continuing Medical Education Credit

Brown Medical School designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through April 30, 2003. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. A high percentage of patients with acute HIV infection commonly present with the following signs and symptoms:
   a) Fever
   b) Lymphadenopathy
   c) Weight loss
   d) All of the above
   e) None of the above

2. The preferred drug for treating all stages of syphilis is:
   a) Acyclovir
   b) Doxycycline
   c) Penicillin G
   d) Ceftriaxone

3. Symptoms of N. gonorrhoeae and C. trachomatis-related urethritis and cervicitis are similar, and easily detectable, in both men and women.
   a) True
   b) False

4. Acceptable treatments for a patient who has both gonorrhea and chlamydia are:
   a) Ceftriaxone 125 mg IM and Penicillin G 7.2 MU IM
   b) Ciprofloxacin 500 mg po and azithromycin 1200 mg po
   c) Penicillin G 7.2 MU IM
   d) Ceftriaxone 125 mg IM and doxycycline 100 mg po bid

5. The immediate response to patients showing TB symptoms should be:
   a) Respiratory isolation and posterior-anterior chest radiographs
   b) Sputum-smear and culture examinations
   c) Respiratory isolation and PPD skin testing
   d) Sputum-smear and culture examinations and posterior-anterior chest radiographs

6. What percentage of acute HBV cases is symptomatic?
   a) 25 - 50%
   b) 50 - 75%
   c) 10 - 20%
   d) 25 - 30%

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**HEPP Report Evaluation**

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1. Please evaluate the following sections with respect to:
   educational value   clarity

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

3. What future topics should HEPP Report address?

4. How can HEPP Report be made more useful to you?

5. Do you have specific comments on this issue?