**About Hepp**

HEPP News, a forum for correctional problem solving, evolved out of ongoing discussions among HIV specialists based at the Brown University AIDS Program about the need for HIV updates designed for practitioners in the correctional setting. The board of editors includes national and regional correctional professionals, selected on the basis of their experience with HIV care in the correctional environment and their familiarity with current HIV treatment. HEPP News targets correctional administrators and HIV/AIDS care providers including physicians, nurses, outreach workers and case managers. Published monthly and distributed by fax, HEPP News provides up-to-the-moment information on HIV treatment, efficient approaches to administering such treatments in the correctional environment, national and international news related to HIV in prisons and jails, and correctional trends that impact HIV treatment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education to physicians who accurately respond to the questions on the last page of the newsletter; please see last page for details.

The editorial board and contributors to HEPP News are well aware of the critical role prisons and jails play in the treatment and prevention of HIV. The goal of HEPP News is to provide reports of effective and cost-conscious HIV care that can truly be implemented within the correctional environment. We hope this newsletter achieves that goal.

**Editors**

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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 beneath the authors’ names.

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

Hepp News is grateful for the primary support of Agouron Pharmaceuticals through an unrestricted educational grant and the additional support of Roche Pharmaceuticals.

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**HCV and HIV in the Correctional Setting**

Anne Spaulding, MD
Rhode Island Department of Corrections

"Hepatitis C is found rife among inmates," trumped a recent New York Times article, (1) a "discovery" that comes as no surprise to correctional providers, since we're well aware of the relationship between drug use, incarceration, and hepatitis C (HCV) infection. Approximately 80% of persons incarcerated in the US admit to a history of using illegal drugs and about 1 in 4 have used parenteral drugs (2). Furthermore, about 4 million non-incarcerated individuals are infected with HCV. Due to the linkages between drug use, HCV, and incarceration, an estimated 1.4 million persons affected by HCV, or 30% of the total HCV cases in the U.S. are believed to pass through correctional facilities each year (3).

The number of incarcerated individuals affected by HCV is high, regardless of the region of the country. For example, Texas reported that 42,000 inmates were infected with HCV (28.6% of the incarcerated population)(1). Other states also report high infection rates among inmates: Connecticut (32%) (4), Virginia (30-40%) (5), Maryland (38%) (6), and California (41%) (7). In New Jersey, 925 inmates were tested for HCV in response to evidence of hepatic transaminase elevations, or co-infection with hepatitis B or HIV. 67.3% of these inmates tested positive for HCV antibody (8). Many states do not formally test for HCV infection in their populations unless medically indicated (for reasons such as elevated liver function tests), therefore, current estimates of the prevalence of HCV infection in some correctional settings may be artificially low.

The prevalence of HCV infection in correctional facilities raises a number of diagnostic and management dilemmas. Unlike HIV infection, which currently requires lifelong treatment after the initiation of therapy, treatment for HCV usually requires intervention for a limited period of time. In addition, many of our patients are incarcerated for relatively brief (and sometimes hard to predict) periods of time. Therefore, it can be difficult to determine whether an individual patient will be able to complete the course of therapy, if it were to be initiated in the correctional setting.

Debate about the timing and location of the treatment course and which budget should bear the cost of treatment (correctional or community), further complicates HCV treatment decisions. And now that patients with HIV are living longer, consideration must be given to treating chronic conditions like HCV that were considered irrelevant to HIV management in the pre-HAART era. Many correctional providers would probably consider the management of HCV and HCV/HIV co-infection in the correctional setting to be their biggest challenge.

**Natural History of HCV Infection**

Hepatitis C virus is a member of the flaviviridae family. Infection is blood borne, and therefore can be associated with injection drug use, tattooing, and needle stick injuries (9). Infection was formerly associated with blood transfusion, until screening for HCV was initiated (1989) and new methods for detecting HCV reduced the risk of HCV transmission by blood products to 1 in 100,000 units.

About 15% of HCV exposed patients resolve their infection without sequelae, while approximately 85% of cases eventually develop chronic hepatitis and persistent although occasionally intermittent, viremia(10). Infection results in the development of closely related yet heterogeneous populations of viral genomes (quasi species). Probably as a result of this genetic diversity, HCV evades the host immune response, leading to a high rate of chronic infection. Persons with chronic HCV are often...
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asymptomatic but have the capacity to infect others. HCV can lead to cirrhosis and liver failure (20% of chronic HCV infections). In people who are co-infected, HIV may cause HCV to advance more quickly; they have a 12 to 30 fold higher risk of developing hepatocellular carcinoma than non-carriers (10). HCV is responsible for approximately 40% of the 25,000 annual deaths from chronic liver disease in the U.S. (9).

• Diagnosis of HCV

Tests that detect antibody against the virus include the enzyme immunoassay (EIA) and the recombinant immunoblot assays (RIBA). The EIA test is suitable for screening for HCV infection. RIBA is used to confirm an EIA result in a low risk population if a positive result is suspected to be a false positive; it probably has little use in a correctional setting. The polymerase chain reaction assay for HCV (RT-PCR) enables direct quantification of the virus in the blood (similar to the HIV viral load assay). A positive RT-PCR is definitive proof of HCV infection. RT-PCR can be used to quantify virus in the course of infection; however, there is variability between laboratories, so clinicians should use the same laboratory to evaluate a patient at sequential time points. Liver biopsy can demonstrate the extent of liver injury. Many gastroenterologists are now questioning the need for routine biopsy in all HCV patients before treatment.

• Treatment Options

In 1997, the National Institutes of Health Consensus Committee recommended treatment of HCV infection with 3 million units of interferon (aIFN) subcutaneously three times a week for 12 months. The 1997 consensus statement, which includes extensive discussions of the natural history of HCV, diagnosis, and treatment, can be found at the following internet website: http://odp.od.nih.gov/consensus/statements/cdc/105/105_stmt.html/

Recent studies indicate important considerations when using interferon. Neutralizing anti-interferon antibodies have been shown to develop in some patients with chronic HCV receiving treatment with interferon. The presence of these antibodies suggests an association with a decrease in responsiveness to interferon (11).

Interferon monotherapy remained the standard treatment for HCV until last year, when the combination of interferon and oral ribavirin won FDA approval because of its improved efficacy. While ribavirin has no lasting effect when taken alone, combining 600 milligrams of ribavirin by mouth twice a day with interferon at 3 million units subcutaneously three times a week leads to a doubling of HCV RNA clearance (10). Most clinicians now initiate treatment with this form of combination therapy, rather than using interferon alone.

Interferon effectively cures between 15 to 20% of patients who are given a one-year course of therapy (9). Combination therapy with interferon and ribavirin has demonstrated 30 to 50% response rates (12, 13, 14). Response to combination therapy may even be observed in patients with advanced HCV infection and cirrhosis (15). The ideal duration of therapy-6 months versus a year-is still being determined. Non-responders to interferon monotherapy can be identified early by assessing the serum ALT level and the presence of serum HCV RNA after 3 months of therapy. If the ALT level remains abnormal, and the serum HCV RNA remains detectable, interferon therapy should be stopped, because further treatment is unlikely to produce a response. If the virus is undetectable, continuation of treatment depends on the HCV genotype (which can be checked before starting therapy). If the virus is genotype 1 (which represents >70% of the HCV in the U.S.), the therapy should be con-

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LETTER FROM THE EDITOR

Dear Colleagues,

In case you were wondering where the newsletter was this month, I have to confess that it went with me to West Africa before it reached the copy desk, hence the delay. That said, I'm really pleased with this issue, because it responds to a concern many of you have voiced in your communications with us. The main article by Dr. Anne Spaulding of the Adult Correctional Institution in Rhode Island, gives her perspective on the management of hepatitis C in the correctional setting. Our guest editor, Lou Tripoli, provides a counterpoint perspective in his editorial. Other features this month include the Hepgram, suggesting treatment guidelines for HCV infection in corrections, and an expert opinion on managing HCV/HIV co-infection by Dr. David Paar of the University of Texas. After reading this issue, readers should understand the scope of hepatitis infection in correctional facilities, list the criteria for HCV treatment in corrections, understand how to adjust the treatment of co-infection, and name which vaccines should be given to hepatitis-infected patients.

Next month, Faye Duffin of the North Carolina Department of Corrections will discuss nurse case management of HIV infection in the correctional setting. We will also provide you with some tools for enhancing nursing management.

Sincerely,
Anne De Groot, MD

EDITORIAL: A RATIONAL APPROACH TO HEPATITIS C INFECTION

We at Correctional Medical Services are responsible for the health-care of about 300,000 incarcerated individuals in United States. We have a great deal of information on the prevalence of diseases within the 32 states in which we operate. Chronic liver disease and cirrhosis rank number 15 on our list of diseases that cause serious medical sequelae. Coronary artery disease, AIDS, diabetes, and a multiplicity of other medical problems consume far more resources and result in far more consequences than hepatitis C.

Why, then, the dramatic new emphasis on hepatitis C in correctional settings? First, hepatitis C tends to be over represented in the inmate population as compared to the general population. Second, the pharmaceutical industry has adroitly seized the opportunity and has been highly successful in driving awareness of hepatitis C both in and outside of correctional institutions. In my opinion, by aggressively treating hepatitis C, we may end up expending valuable resources providing medication to a large number of people who may derive no substantial benefit, in order to prevent complications in a minority. Many of us believe that new therapies will become available in the future to treat this infection, and that new strategies will emerge to better predict which patients will benefit from treatment.

I beg my colleagues to pursue a rational approach to hepatitis C infection, somewhat like the one Dr. Spaulding describes in this issue. However, I would be even more conservative in my approach. Much of what we believe about hepatitis C comes to us from content-area specialists, such as hepatologists, few of whom have had any appreciable experience treating a correctional population. No long-term studies are available to tell us whether those who are selected for treatment in correctional settings will benefit from treatment and maintain behaviors that will reduce the chance of future reinfection.

Are we being led down a “primrose path” by the drug companies? Certainly, a great deal of human suffering has been alleviated by the development of new pharmaceuticals. I have yet to see any of the pharmaceutical companies offer to cut their prices for the medications that they sell to the prisons for the treatment of hepatitis C. I have also yet to see any of them make this medication available to these same people who, when outside of the prison, are unable to get any medications at all.

Given that most people infected with hepatitis C virus had a long interval to wait for the development of cirrhosis, I would hope that we exercise rationality in the application of the available technology to this infection. We should discard the scientific and the rational for the expedient. Whether we care to recognize it or not, every action we take costs something in the form of missed opportunity in action we did not take.

Sincerely,
Louis C. Tripoli, MD
Vice President of Medical Affairs
Correctional Medical Services, St. Louis, Missouri
Adjunct Assistant Professor of Medicine
Johns Hopkins University

Dr. Tripoli recommends the following article for further discussion of HCV treatment: Editorial: Making sense of Hepatitis C. Lancet, 1998 Nov 7. Please take a moment to write the editors back. Tell us whether HEPP News is working for you and please feel free to respond to any of the articles or editorials by e-mail to heppnews@brown.edu or fax to Betsy Stubblefield at 401.863.1243.

SAVE THE DATES

1999 National HIV Prevention Conference
August 29 – September 1, 1999
Atlanta, Georgia
For more information, call 404.639.1942, or e-mail: 99hivconf@cdc.gov

1999 HCV Global Foundation 3rd Annual HCV Conference: The World and Hepatitis C
August 21-23, Oakland, California
Contact: Ronald Duffy - HCV Global Foundation
707.425.8862, Fax 707.425.8862 or visit www.hcvglobal.org

Clinical Trials in the Correctional Setting
Providence, Rhode Island
October 13-15, 1999
Conference will review the practice and legal and ethical aspects of clinical trials in correctional settings. Will develop practical guidelines from the perspective of institutions where trials are being held. Contact Betsy Stubblefield via fax 401.863.1243 or e-mail heppnews@brown.edu

HIV/AIDS Behind Bars
Call for Abstracts
HEPP News at BRUNAP is sponsoring a pre-conference colloquium on November 7 at the NCCHC conference listed above that will discuss public health and corrections collaborations. Accepting 500 word abstracts addressing this topic until September 1. Please fax (401.863.2180) or e-mail (heppnews@brown.edu) questions to Betsy Stubblefield.

23rd National Conference on Correctional Health Care
November 8 - November 10, 1999
Fort Lauderdale, Florida
For more information, call 773.880.1460
Fax: 773.880.2424 Or visit: http://www.ncchc.org

1999 ACA 129th Summer Congress of Correction
August 9-12, 1999
Denver, Colorado
For more information, visit http://www.corrections.com/acacconference/colorado99/index.html
To register by phone: 1.800.222.5646 ext.1922; or by fax: 301.918.1900

HEPP News is published twelve times a year by the HIV Education/Prison Project at the Brown University AIDS Program
Box G-B426, Brown University, Providence RI 02912
Tel: 401.863.2180 Fax: 401.863.1243
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Despite these caveats, there is emerging evidence that treating HCV in HIV co-infected patients may prevent liver failure. Outcomes may improve further since the recent approval of ribavirin in combination with interferon as standard initial HCV therapy. An AmFAR sponsored study of interferon with or without ribavirin therapy in HIV/HCV co-infected patients has been ongoing since 1998. Anemia, which causes treatment withdrawals in some HCV-infected patients may be a significant problem when the combination is used in patients with HIV especially when HIV, is advanced or AZT is used. Thus, treatment of HCV is now being carefully considered for selected HCV-infected incarcerated patients. The challenge for the correctional physician lies in determining whether treatment is appropriate for an individual patient.

• Timing and Cost Effectiveness

HCV cure rates (sustained virologic response) with currently available regimens remain low, ranging between 15 to 50%, depending on the treatment (12, 13, 14). The cost of the medication can be as high as $12,000 per year per patient. Low cure rates and high cost have led to delays in the initiation of HCV screening programs in correctional settings, even though screening for and treating HCV has been shown to be cost-effective in some populations. For older patients, a 6 month-long treatment was on the scale of other interventions that the American public would accept. For young patients, 6 months of treatment maybe cost saving (23). The use of ribavirin for HCV changes the picture-cost benefit analyses for combination therapy. Combination therapy is more expensive than interferon alfa alone, but because it has a higher success rate, it may be more cost-effective.

Careful selection criteria can further improve the cost-effectiveness of HCV treatment in the correctional setting. My colleagues and I have previously shown that a policy of routinely treating appropriately screened HCV patients with interferon treatment demands only 3% of correctional facility health care budgets (24). The following table shows the hepatitis treatment criteria at RI DOC with the addition of criteria that must be met before adding ribavirin to a regimen.

Proposed Inclusion Criteria for Hepatitis Treatment in Prisons Adapted from RI DOC Criteria and California DOC

- Rule out other causes of liver disease (hemochromatosis, Wilson’s disease, autoimmune hepatitis, and alpha-1 antitripsin deficiency)
- Hepatitis virus detectable by PCR
- No alcohol or parenteral drug use in preceding 6 months
- Enroll in a substance abuse program if history of drug/alcohol use
- Control of major illnesses, including HIV (CD4 usually > 400 cells/ml)
- Good control of any psychiatric illness, especially depression
- Length of stay in prison > 15 months from initiation of treatment
- No signs of decompensated liver disease
- Transaminases greater than upper limits of normal
- Platelet count > 75,000
- Hematocrit > 30%,Albumin > 3.5 mg/dl,Creatinine < 1.5 mg/dl, INR< 1.2
- Thyroid function tests NL, no elevated autoantibody titers (ANA, AMA)
- Before treatment with ribavirin: No evidence of coronary heart disease. Birth control, if conception possible (men and women). Willingness to submit to monthly pregnancy tests (women).

Many U.S. inmates may meet the criteria described above and receive treatment, however, the total number of HCV infected inmates treated using these criteria will be much lower than the total number of inmates who have HCV infection. One approach to limiting the impact of HCV screening on correctional budgets might be to screen only those inmates who would qualify for HCV treatment by clinical criteria. Appropriately screening HIV patients for treatment may reduce HCV treatment costs.

Hepatitis B (HBV) - Overlooked and Under-treated

The prevalence of chronic HBV (HBsAg positive patients) may be lower than HCV infection in correctional settings, but it is still a threat. In fact, HBsAg positivity rates (up to 47%) are considerably higher than in non-incarcerated populations (5%).

• Vaccination and Screening for HBV

Prisons are an ideal setting for HBV vaccination, although only a few facilities have adopted CDC guidelines recommending that the following receive HBV vaccine: exposed personnel, pregnant women, and house- and sexual contacts of HBsAg carriers (26). The CDC has also recommended HBsAg screening for all pregnant women, and vaccination is recommended for the household and sexual contacts of HBsAg carrier. Correctional facilities can obtain HBV vaccine for free for inmates patients up until their 19th birthday under a federal program, Vaccines for Children. Accessibility may differ in each state but providers can check with local departments of health, which may be willing to consider cost sharing for HBV vaccination for older inmates, depending on the region’s incidence of HBV infection. HBV vaccination has been adopted in some correctional facilities due to the high rate of infection among inmates returning to correctional facilities. In Rhode Island, incidence of new HBV infection in recidivist women has been demonstrated to be high: 12 per 100 person years. This year, RI DOC began vaccinating inmates less than 19 years old (27). HBV vaccination is less effective in patients who already have HIV infection, thus boosters or higher doses may be needed (28).

• Treatment Options for HBV

Interferon at 5 million units subcutaneously for 16 weeks was the first treatment for chronic HBV infection. New agents for HBV, including lamivudine (3TC), adefovir (ADV) and famciclovir (Famvir) are in the process of being evaluated. Each patient should be evaluated for treatment and decisions about treatment should be made on an individual basis.

• Treatment of HBV in the Presence of HIV Co-infection

HIV may lessen the liver damage in the HIV/HBV infected patient and treatment could be less of an issue than with HCV/HIV co-infection. If, in the future, life expectancy for HIV increases further, even moderate liver damage in HIV/HBV co-infected patient may need to be addressed, especially if HBV treatment improves. Whether sequential or combination therapy is optimal is unclear. Any liver damage at all may be important if it will compromise tolerance of anti-retroviral therapy.

Contributors include: HEPP Staff and Rob Lyerla, PhD, epidemiologist in the Hepatitis Branch, National Center for Infectious Diseases, CDC.

• Conclusion

High HCV infection rates and new guidelines for treatment are forcing difficult decisions in correctional health facilities. In community settings, clinicians treat HCV infected patients who meet treatment criteria with combination interferon/ribavirin therapy. Guidelines for the selection of patients for therapy in correctional settings should be developed, with the participation of regional public health officials. Cost-sharing between correctional facilities and public health is a subject that needs to be explored, particularly if 30% of all people with HCV in the community cycle through correctional facilities. Treatment of these individuals to reduce HCV morbidity and mortality will have broad implications for general public health.

Treatment of HCV infection in HIV infected patients also bears careful consideration. As HAART therapy continues to prolong the lives
HEPPigram

A feature of HEPP News providing concise solutions to correctional HIV-related problems.

Before Starting Therapy

- Diagnosis suggested by aminotransferase (ALT or AST) elevations. Confirm using HCV antibody and HCV RNA levels.
- Rule out other causes of increased hepatic transaminases. Obtain hepatic ultrasound. At a minimum, obtain iron studies, alpha fetoprotein level, PPD, hepatic ultrasound, copper levels.
- Consider a liver biopsy to confirm HCV diagnosis, assess the grade and stage of disease, and rule out other diagnoses. Biopsy remains controversial as antibody testing, HCV RNA and liver synthetic function assays are probably just as accurate.
- Assess for suitability of therapy and contraindications (stable mental illness, no decompensated cirrhosis, sufficient sentence to complete therapy)
- Test for HCV genotype (or serotype) to help determine the duration of therapy.
- Measure CBC, AST, ALT, albumin and prothrombin time to establish a baseline for these values.
- Counsel the patient about the relative risks and benefits of treatment. Side effects and contraception should be thoroughly discussed.

During Therapy

- Start therapy with interferon 3 million units by subcutaneous injection thrice weekly plus RBV 1,000 or 1,200 mg p.o. daily (may be in BID divided doses).
- At weeks 1, 2, and 4 and then at intervals of every 4 to 8 weeks thereafter, assess side effects, symptoms, CBC, PT, albumin and AST/ALT.
- Adjust the dose of RBV downward (by 200 mg at a time) if significant anemia occurs (Hgb < 10 gm/dL or Hct < 30%) and stop RBV if severe anemia occurs (Hgb < 8.5 gm/dL or Hct < 26%).
- At 24 weeks, assess HCV RNA levels. If HCV RNA is still present, stop therapy. If patient had genotype 1 (1a or 1b) and HCV RNA is negative continue therapy for another 24 weeks. If HCV RNA is non-detectable, continue therapy for a total of 48 weeks. For those with genotypes 2 and 3, stop therapy if HCV RNA is not lowered. Recheck HCV RNA level at the end of treatment.
- Measure thyroid-stimulating hormone levels every 3 to 6 months during therapy.
- Reinforce the need to practice strict birth control during therapy and for 6 months thereafter.
- At the end of therapy, test HCV RNA level to assess whether there is an end-of-treatment response.

After Therapy

- Measure AST/ALT levels every 2 months for 6 months. In responders, repeat HCV RNA testing 6 months after ending therapy.
- Six months after stopping therapy test for HCV RNA. If HCV RNA is still negative, the chance for a long-term “cure” is excellent; relapses have rarely been reported after this point.

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of HIV infected people, providers need to place more importance on co-morbid conditions. More HIV patients may die from illnesses other than opportunistic infections. We recommend that all HIV infected patients receive screening for viral hepatitis antibodies (but screening does not need to take place during incarceration, especially if the stay is brief).

Correctional facilities with limited budgets are urged to develop guidelines for prioritizing whom will receive HCV therapy. We recommend that HCV/HIV co-infected patients who have participated in substance abuse treatment, have an expected duration of incarceration that permit completion of therapy, have stable psychiatric or medical conditions, have elevated transaminases but normal hematological parameters, be considered for treatment of hepatitis C virus.

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6. Personal communication, Stanley Ostrawski, RN, MS MT. ASCP, CIC Statewide Infection Control Coordinator Correctional Medical Services Mt. Laurel, NJ.
7. Ruiz JD, Mikanda J. Seroprevalence of HIV infected people, providers need to place more importance on co-morbid conditions. More HIV patients may die from illnesses other than opportunistic infections. We recommend that all HIV infected patients receive screening for viral hepatitis antibodies (but screening does not need to take place during incarceration, especially if the stay is brief).
8. Personal communication, Stanley Ostrawski, RN, MS MT. ASCP, CIC Statewide Infection Control Coordinator Correctional Medical Services Mt. Laurel, NJ.
25. Personal communication, Rob Lyerla, PhD, epidemiologist in the Hepatitis Branch, National Center for Infectious Diseases, CDC.
Ask The Expert

Jim is a 38-year old who was diagnosed with HIV in 1989 and with HCV in 1996. After release from prison twelve years ago, he began using injectable drugs. He has been clinically diagnosed with depression however has resisted antidepressant therapy or counseling. Since his diagnosis, he has started and stopped antiretroviral medications (AZT, d4T, ddl, ddC, 3TC) several times while in the community. Indinavir was discontinued after one month in 1997 secondary to hyperbilirubinemia. In 1998, he began AZT, 3TC and nevirapine consistently, however he describes becoming progressively more depressed and bingeing on alcohol. In early 1999, he is incarcerated and reports recent injection cocaine use and is admitted to your jail and is given his AZT/3TC/nevirapine regimen.

Four weeks after admission, his vital signs are normal and has poor eye contact. He is noted to have oral thrush. His abdominal exam demonstrates a normal liver size (9cm) without evidence of ascites. Occasional spider telangectasias are noted on his trunk. Neuropsychiatric evaluation reveals suicidal ideation without active plans. His laboratory studies reveal an HIV-1 RNA of 43,000 copies/mL and CD4 = 43. His other routine laboratory findings include a WBC=3,600, platelets=40,000, HGB=11.5, MCV=106, ALT=47, AST=39, PT=13.2 and albumin=3.8.

What is more likely to be an immediate concern for this patient--HIV or HCV? What regimen would you suggest to treat his HIV? Is he a candidate for HCV treatment?

What Would You Do?

David Paar, MD,
Assistant Professor of Medicine,
University of Texas Medical Branch at Galveston
Speaker's Bureau: Roche Pharmaceuticals;
Education Grant: Merck Immune Response Corp.,
Other Support: Glaxo Wellcome, Pfizer

Before answering the specific questions at the end of the case presentation, I think it would be useful to review the role that psychiatric disorders play in HIV infection. Co-morbid mental illness may be a contraindication to interferon therapy for HCV and is correlated with poor adherence to antiretroviral therapy. For example, untreated depression may lead to feelings of hopelessness and despair, or patients may treat their depression with alcohol and other substances that can directly lead to poor adherence. This may lead to multi-drug resistant HIV and possibly high risk behavior associated with HIV transmission. I have heard more than one HIV psychiatrist assert that psychiatric illness is what is driving the HIV epidemic in the 90s. I think Jim's psychiatric co-morbid conditions need to be properly diagnosed and treated as part of his comprehensive HIV care.

The good news for Jim is that he has three treatable medical conditions: HIV, HCV and depression. It is the complexity of this patient's co-morbid conditions that create the challenge. In this case, he is presenting with late stage HIV infection (CD4<50) which, left untreated, has a mortality risk of 25% within the next six months. Jim has no significant evidence of hepatic synthesis dysfunction and his transaminases are minimally elevated. Therefore, Jim's HCV is less problematic at this point and his risk for cirrhosis from HCV is 10% per decade. An important intervention would be to carefully reintroduce a potent antiretroviral combination. If his HIV is appropriately managed, he may then live long enough to experience the complications of HCV infection - cirrhosis or hepatocellular carcinoma.

What regimen would I suggest to treat his HIV? I would need more details in order to provide the best answer. For example, the current regimen might be partially effective if, for example, the baseline HIV-1 RNA was 400,000 copies per ml or greater, in which case the current viral load would represent a significant reduction (1.0 log) in response to treatment. It would also be helpful to know the extent of exposure to the other nucleosides because these could be recycled if the duration and pattern of drug administration did not promote clinically significant resistance. For the purposes of this case, it is likely that this patient has complete resistance to all non-nucleoside RTIs because of the rapid resistance that develops to this class of drugs. He is likely to have a 184 mutation associated with 3TC resistance as well. The other RTIs are an altogether different issue and their resistance is dependent on the duration of their previous use. His adherence history suggests that he may be able to recycle one or more of these agents with ddI and d4T being the least likely to develop resistance rapidly.

Of course, I'm presuming a lot, and would therefore order a genotypic/phenotypic assay to guide therapy. If genotyping were not available, I would likely use a two protease combination (RTV+SQV, RTV+IDV, or NFV+SQV) with two or more additional recycled nucleoside analogues. Recycled nucleosides that might be used could be ddI+d4T; if ddI were used, I would consider adding hydroxyurea one to three months after initiating the regimen in order to obtain the initial increase in CD4 count that would be blunted if hydroxyurea were used up front. If genotyping did not demonstrate multiple mutations for the class of RTIs, I would use abacavir as one of the RTIs. This patient would need very close monitoring as the complex regimen could create multiple side effects that would need prompt attention in order to sustain this patient on antiretroviral therapy.

Is he a candidate for HCV treatment? Since I'm not an HCV treatment expert, I would consider referring him to a hepatologist for evaluation. Such diagnostic measures as quantitative HCV RNA, liver biopsy for histopathologic examination, and serial hepatic transaminase determinations would aid in making treatment recommendations. The combination of interferon with ribavirin has yielded impressive results in HIV uninfected patients with 50% achieving sustained remission. Similar studies in HIV infected patients are in progress. Until this patient has achieved a remarkable increase in CD4, it would be unlikely that he would achieve adequate results with the combination suggesting that immune reconstitution after HIV treatment would be essential before considering HCV therapy. Moreover, Jim would not be a candidate currently because of his untreated depression.

In summary, Jim's depression and substance use need to be addressed so that he is able to adhere to long-term, effective antiretroviral therapy. If his HIV remains untreated, he will die of complications of HIV in the short term; if he receives effective antiretroviral therapy that delays or prevents HIV-related mortality, he will be at risk for the long term complications of HCV infection. Designing an effective antiretroviral regimen will require additional history and good clinical judgement; resistance assays would be useful in making a final decision. Finally, while there are some relative contraindications to HCV therapy, Jim may be a candidate for treatment once his psychiatric illnesses and HIV infection are adequately treated.
New Interferon Reaches Same Blood Level in Cirrhotic and Non-Cirrhotic Patients.
An investigational study found that a longer-lasting term of interferon alfa-2a (Roferon-A; Hoffman-La Roche, Nutley, NJ) reaches the same blood levels as non-cirrhotic patients then administered once-weekly in cirrhotic patients. *Hepatology* 1997; Vol 26(3) (Suppl-1).

Mandatory Inmate HIV Testing Rejected
A proposal that would make HIV testing mandatory in Maine correctional institutions was rejected by the State Senate by a vote of 21-13. A Bar Harbor legislator and nurse, Jill M. Goldthwait, said hospitals do not require the procedure and neither should prisons. According to Sen. John W. Benoit, (R) the concept is not recommended by the National Centers for Disease Control because it is not based on risk factors and the idea could create a false sense of security. (June 6, 1999. *Bangor News*)

Viral Reservoirs: Two Studies Confirm HIV Persistence Despite HAART
Two new studies (Zhang et al., Furtado et al, *NEJM* 5/27/99) add to the growing evidence that even when highly active antiretroviral therapy (HAART) pushes HIV to undetectable levels, the virus hides in the body and continues to replicate.

Resources / Opportunities

Center for Substance Abuse Treatment’s (CSAT) Comprehensive Community Treatment Program (CCTP)
CCTP is a “Knowledge Development” initiative, requiring the application of rigorous evaluation/research methods to develop new knowledge about approaches to substance abuse treatment, and emphasizing three aspects of treatment: 1) special populations, 2) integrated substance abuse treatment, screening, and early intervention in non-traditional settings, and 3) innovative programs. Due dates: 9/10/99, 1/10/00, 5/10/00. The announcement and application materials are available at SAMHSA’s website: www.SAMHSA.gov
Contact: NCADI 800.729.6686. E-mail: info@health.org

NMAC’s Equal Access Initiative Computer Grants Program
The announcement and further details are available at www.nmac.org. Or call Peter Velasco at NMAC: 202.483.6622 or e-mail: pvelasco@nmac.org.

Hepatitis Education for Inmates and Correctional Staff
Program announcement 99145. Contact: Linda Moyer at 404.639.2709 or e-mail: Lam1@cdc.gov. More information is also available at http://fundingopps2.cos.com/

Technology Translation and Transfer of Effective HIV Behavioral Interventions. Centers for Disease Control Program Announcement 99089. Contact: Robert Kohmescher at 404.639.1914 or e-mail: rnk1@cdc.gov.

Resources:
Patients’ Guide to HIV Medicines and Guidelines for Their Use
This publication from the National Minority AIDS Council provides clear and accurate guidelines for the use of HIV medications and also lists other sources of information on HIV/AIDS. It is available online at the AIDS Treatment Information Service (ATIS) website: www.hivatis.org. Free copies are also available from HIVATIS at 800.448.0440; TTY 888.480.3739.

Internet Resources:

HIV and Corrections-Related:
National Commission on Correctional Health Care: http://www.ncchc.org
National Library of Medicine:
Harvard AIDS Institute: http://www.hsph.harvard.edu/hai/home.html

HCV-Related:
Hepatitis Information Network: http://www.hepnet.com
HIV & Hepatitis: http://www.hivandhepatitis.com
Hepatitis Weekly: http://www.newsfile.com
Hepatitis C Website:
Links to hepatitis websites: http://www.asf.org/hepatitislinks.html
National Institute of Allergy & Infectious Diseases:
http://www.niaid.nih.gov/dmid/hepcframe.htm
http://www.niaid.nih.gov/dmid/hepatitisc.htm

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Self-Assessment Test for Continuing Medical Education Credit

Brown University School of Medicine designates this educational activity for 1 hour in category 1 credit toward the AMA Physician’s Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through September 15, 1999. The estimated time for completion of this activity is one hour and there is no fee for participation in this activity.

1. Each of the following patients has chronic hepatitis C with anti-HCV and HCV RNA in serum and liver biopsy showing chronic hepatitis. Indicate which of the following individuals would be reasonable candidates for alpha interferon therapy.
   Y/N 69-year old renal transplant with abnormal ALT levels (105 U/L), 18 month sentence.
   Y/N 25 year old injection drug user who has no history of drug rehabilitation and will be released in two months.
   Y/N 30 year old HIV infected individual with CD4< 250 cells/mL, two year sentence.
   Y/N 30 year old with normal thyroid function tests, sentence 16 months, absence of advanced cirrhosis on liver biopsy.

2. The recommended dose of alpha interferon and oral ribavirin therapy for chronic hepatitis C is:
   a) 600 mg ribavirin orally twice a day and 3 million units IFN subcutaneously three times a week.
   b) 400 mg ribavirin orally twice a day and 5 million units IFN subcutaneously three times a week.
   c) 600 mg ribavirin orally twice a day and 3 thousand units IFN subcutaneously three times a week.
   d) 600 mg ribavirin orally and 3 million units IFN subcutaneously daily.

3. The appropriate means of documenting a long-term response to alpha interferon therapy of chronic hepatitis C is:
   a) liver biopsy at the end of treatment
   b) testing for aminotransferase and HCV RNA at the end of treatment.
   c) Liver biopsy done 6 to 12 months after stopping treatment
   d) Serum testing for aminotransferases and HCV RNA 6-12 months after stopping treatment.

4. Recommendations to patients co-infected with HIV and chronic hepatitis C should include:
   a) have sexual partner(s) checked for anti-HCV
   b) avoid taking ddI/ribavirin
   c) receive hepatitis A vaccine
   d) receive hepatitis B vaccine
   e) a, c and d
   f) all of the above

5. A patient infected with HCV genotype 1 is checked after 6 months of combination therapy for HCV aminotransferases. No virus is detected and transferases are normal. Therapy should be stopped.
   a) Yes, because if the virus is undetectable, therapy can be considered complete.
   b) No. Because the patient has HCV genotype 1, therapy needs to be continued.

6. The CDC has recommended hepatitis B vaccine for the following individuals:
   a) all pregnant women
   b) household and sexual contacts of HbsAg positive individuals
   c) exposed personnel
   d) persons co-infected with HIV and HCV
   e) a, b and c
   f) all of the above

HEPP News Evaluation

1. Please evaluate the following sections with respect to:
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   main article 5 4 3 2 1  5 4 3 2 1
   HIV 101 5 4 3 2 1  5 4 3 2 1
   HEPPigram 5 4 3 2 1  5 4 3 2 1
   updates 5 4 3 2 1  5 4 3 2 1
   resources 5 4 3 2 1  5 4 3 2 1

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3. What future topics should HEPP News address?

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July 1999 • Volume 2, Issue 7  visit HEPP News Online at www.hivcorrections.org