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PRISON
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HCV IN CORRECTIONS: FRONTLINE OR BACKWATER?

Rebecca Nerenberg*, B.A., Managing Editor, HEPP News, Michael Wong, M.D., Harvard Medical School and Anne De Groot***, M.D., Brown Medical School**

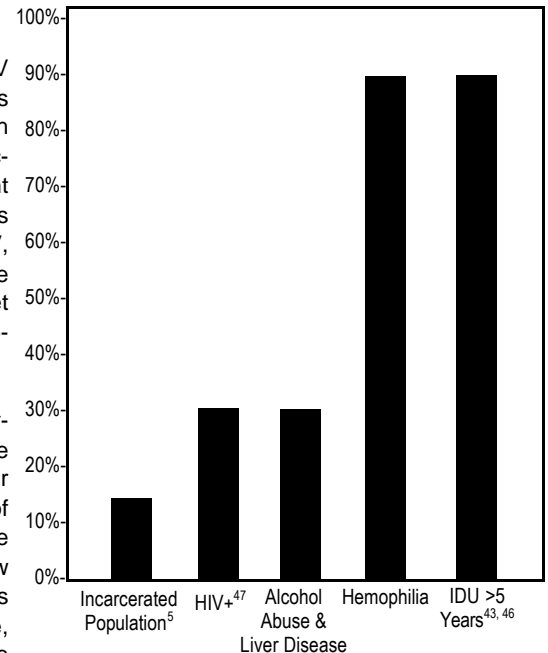
Nationally, hepatitis C virus (HCV) outstrips HIV by about 10 to 1 in sheer numbers of inmates infected. Even so, controversy and confusion surround the management of HCV in correctional settings, while HIV testing and treatment is now relatively routine. This controversy stems from debate about the "best time" to treat HCV, and whether HCV treatment should begin to be included in the correctional health care budget or whether the cost should be borne by the public health sector.

While the debate about HCV treatment in corrections continues, significant advances in the treatment of HCV have occurred, and a number of correctional systems are taking advantage of this opportunity to intervene. Will improved care and accelerated implementation of the new therapies lead to diminished health care costs in years to come? Only time will tell. Meanwhile, education, testing, and prevention must be paramount. As has been observed for HIV, programs that test and educate inmates about HCV may lead to a reduction in the transmission of HCV after inmates are released into the community.

HCV EPIDEMIOLOGY

It has been estimated that 1-2% of the general population (2.9 to 5.8 million people) in the United States has been exposed to HCV¹, with 75% to 85% developing chronic HCV infection. The behavior that puts people most at risk for exposure to HCV is intravenous drug use (IDU). Other risks include use of shared injection equipment including cotton filters and "cookers,"² unprotected sex with an HCV-infected partner (3%-13% lifetime risk), and receipt of blood products prior to 1988. Prevalence rates in certain high-risk groups are as high as 90% (Figure 1). Since so many of the behaviors that put people at risk for developing HCV infection also put them at risk for incarceration (ie IDU), it should not be surprising that HCV is common in the correctional setting.

FIGURE 1: HCV Prevalence in High Risk Populations



INMATES AT RISK

The most comprehensive analysis of HCV in the correctional system was compiled by Ted Hammet of Abt Associates in the context of a report for the NIJ and the NCHC's report to Congress.⁵ In this report, the researchers estimated that approximately 30% of the total US population living with chronic HCV was released from prisons and jails in the US in 1996 (1.0 to 1.25 million people). The overall prevalence of HCV infection among inmates is estimated to be about 17% nationally, almost 10 times higher than the estimated 1.8% prevalence in the general US population.⁶ In certain sub-populations of inmates (ie those who are HIV-positive or who have abnormal liver function tests) the HCV prevalence can be even higher. Furthermore, the HCV/HIV co-infection

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rate is about a third higher in incarcerated women than incarcerated men, which reflects womens' participation in HCV and HIV risk behaviors.⁴

HEPP News recently performed a survey to assess the current practices regarding HCV management in state correctional facilities.⁷ Based on preliminary data from this study, the prevalence of HCV in inmate populations ranges between 9% and 39% by state (Figure 2).

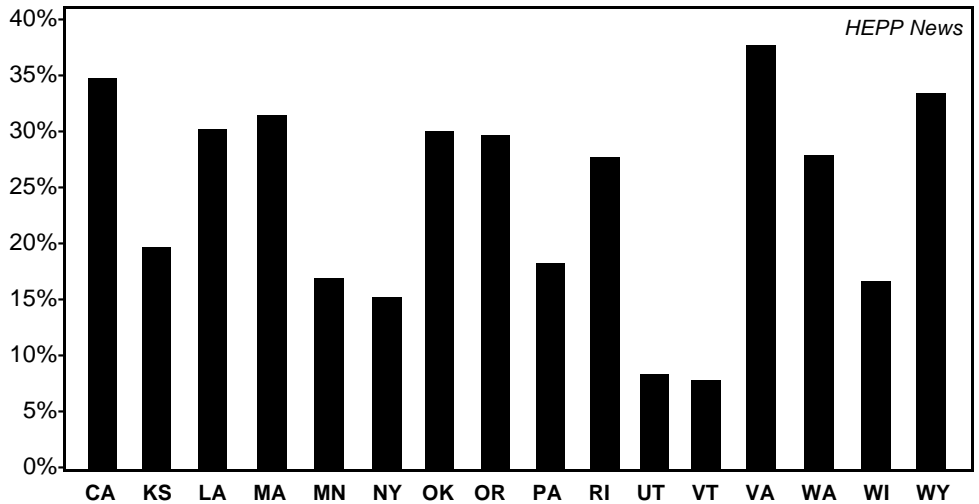
TARGETED SCREENING

Approximately 50% of persons with chronic HCV are unaware of their infection.⁵ Only about 2/3 of chronically infected individuals develop symptoms of infection, and these symptoms are often non-specific malaise and fatigue.⁸ The CDC states that "[t]esting persons in settings with potentially high proportions of injecting-drug users (e.g., correctional institutions, HIV counseling and testing sites, or drug and STD treatment programs) might be particularly efficient for identifying HCV-positive persons."⁹

Cost associated with HCV screening can be reduced by focusing on certain sub-populations that have particularly high prevalence of HCV infection (see HEPP News April 2001 p2).¹⁰ There are a variety of tests available for diagnosing HCV. Enzyme immunoassay (EIA) is the most cost-effective screening test; recombinant immunoblot assay (RIA) helps confirm positive EIA results, while polymerase chain reaction (PCR) is the "gold standard" for confirming active HCV infection with viral replication. In rare cases, the HCV antibody tests can give false negatives. Repeat antibody or viral load testing may be necessary when there is a significant suspicion of HCV infection in HIV infected patients, as low CD4 T cell counts have also been associated with false negative HCV antibody and PCR tests.^{8, 11, 12}

Testing for hepatitis infection informs the patient and physician about the potential for and possible existence of liver damage, and it should serve as an important prompt for a discussion about risky behaviors (particularly if the patient is not yet HCV infected), of factors associated with more rapid progression of HCV disease (such as alcohol abuse) and about the potential for transmission to others.¹³

FIGURE 2: Percentage of HCV-Positive Inmates By State, 2002



HCV prevalence as estimated by experts working with state correctional systems. These data were collected by HEPP staff who contacted correctional medical decision-makers in 30 states. (Jang, Nerenberg, De Groot, Unpublished data from telephone survey conducted Oct 2001-Feb 2002.)

TABLE 1: SVR[†] Rate According to Weight-Based Ribavirin Dosing and Type of Interferon

	Pegylated Interferon [^]	Standard Interferon ^{^^}
All patients		
Overall	54% (274/511)	47% (235/505)
Ribavirin dose ≤10.6 mg/kg	50% (160/323)	27% (6/22)
Ribavirin dose >10.6 mg/kg	61% (114/188)	47% (229/483)
Genotype 1		
Overall	42% (145/348)	33% (114/343)
Ribavirin dose ≤10.6 mg/kg	38% (87/226)	20% (3/15)
Ribavirin dose >10.6 mg/kg	48% (58/122)	34% (111/328)
Genotype 2 or 3		
Overall	82% (121/147)	79% (115/146)
Ribavirin dose ≤10.6 mg/kg	79% (70/89)	50% (3/6)
Ribavirin dose >10.6 mg/kg	88% (51/58)	80% (112/140)

[†]SVR= sustained virologic response [see "Expected Outcome" on page 4]
[^] (PEG-Intron, Schering) 1.5mg/kg/ wk for 48 weeks; ^{^^}3 MIU 3x/wk for 48 weeks
 From Manns, et al. Lancet. 2001; 358: 958-965.¹⁶

WHO SHOULD GET TREATED?

A number of correctional facilities have developed protocols for deciding which patients should consider initiating treatment while incarcerated (HEPP News, April 2001).¹ HHS recommends antiviral treatment for "patients with chronic hepatitis C who are at greatest risk for progression to cirrhosis. These persons include anti-HCV-positive patients with persistently elevated ALT levels, detectable HCV RNA, and a liver biopsy that indicates either portal or bridging fibrosis or at least moderate degrees of inflammation and necrosis."³⁰

SHIFTING STANDARDS FOR TREATMENT OF HCV

Pegylated interferon is the latest advance in HCV treatment (FDA approved, 2001).

The standard interferon alfa has been conjugated to a molecule of polyethylene glycol (PEG), which has increased the half-life of the interferon. Pegylated interferon can be given as a once-weekly injection in contrast with the three-times weekly injection of standard interferon alfa.

For those HCV-positive inmates who are going to be treated, initial treatment of chronic HCV with ribavirin/pegylated-interferon alfa is rapidly becoming the standard of care due to improved outcomes (see Table 1), when compared to standard (non-pegylated) combination therapy.¹⁶ This will be a significant change from years past, when standard (non pegylated) interferon alfa, in combination with ribavirin, was the standard of care.

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1. See protocol developed by Lou Tripoli and colleagues for CMS in HEPP News, April 2001, p.6 for example

LETTER FROM THE EDITOR

Correctional Physicians in a Quandary about Hepatitis C Treatment

As the main article shows, even experts cannot agree on specific criteria for Hepatitis C treatment eligibility. Consensus is emerging that abnormal liver function tests do not preclude progression of cirrhosis in certain patients. Consequently, some say that only biopsy changes, not liver function tests, can be used as a guide to treatment eligibility. More and more evidence is appearing in the literature supporting the performance of liver biopsies in nearly all cases of HCV infection. In corrections, these tests are expensive and logistically complicated. The correctional physician is caught in a vise-like dilemma between the clamor for more HCV diagnosis and treatment and the lack of established criteria predicting who would benefit from these expensive therapies.

Drug availability is also an issue. Currently, PEG-Intron (Schering-Plough) is not available immediately to all patients who are prescribed treatment. While a number of correctional systems are prescribing PEG-Intron to inmates, there seems to be a substantial difficulty in securing sufficient supplies of this drug for both correctional and non-correctional patients.

In response to the shortage, Schering devised the Access Assurance Program. The prescribing clinician must fill out forms and request the patient to be enrolled in the Access Assurance. After acceptance, the patient may have to wait variable periods, up to 11 weeks, to receive the first dose. Once started, however, Schering guarantees uninterrupted access to PEG-Intron for the duration of the treatment. At time of this writing, there were still shortages of PEG-Intron and a waiting list. In prison systems, where inmate transfers between institutions are frequent, the inability to keep stocks of PEG-Intron poses a serious logistical problem. Inmates may arrive to an institution without their PEG-Intron. It may take several days to secure the inmate's allocated PEG-Intron from Schering-Plough.

This is a good time to remind ourselves to keep informed about these rapid developments and to network with other correctional physicians in mutual support. Our patients deserve no less.

This article will review the status of HCV management in correctional settings, provide new information on the interaction between HIV infection, HIV treatment, and HCV, and review guidelines on the management of HCV in HIV infected patients.

Joseph Paris, M.D.

Published monthly and distributed by fax, HEPP News provides up-to-the-moment 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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The standard regimen now consists of daily oral ribavirin (usually five to six pills divided into two doses) and once-weekly pegylated alfa-interferon injections (dosed by weight; see HCV 101 for dosing and side effects of treatment regimens). Standard interferon and/or monotherapy are currently only used if the patient cannot take pegylated interferon or ribavirin due to toxicities or side-effects (see Box 1 for anti-HCV drugs).

EXPECT DELAYS

Currently, PEG-Intron (Schering Plough) is not available immediately to all patients who are prescribed treatment. Because demand has exceeded supply, the company has developed the "Access Assurance" program to ensure that all patients who begin PEG-Intron treatment can successfully complete it.¹⁸ A second pegylated interferon alfa (Pegasys, Roche), is expected to be approved by the FDA in the second half of 2002. This product will also require once-weekly injections. Roche is expected to release its own ribavirin along with Pegasys.

LENGTH OF TREATMENT

Recommendations related to the duration of combination therapy depend on viral genotype. Genotypes 1a, 1b, 2, and 3 are the most common in the United States; 70% to 80% of patients are infected with genotype 1. 8 Recommendations are:

- ◆ HCV genotype 1: A 48-week (12-month) course of therapy.
 - ◆ HCV genotype 2 or 3: A 24-week (6-month) course of therapy.
- Interferon monotherapy is no longer the standard of care for initial therapy.

EXPECTED OUTCOME

The goal of HCV therapy is to obtain a sustained virologic response (SVR), which implies that HCV RNA remains undetectable for 6 months or more after therapy stops. This correlates with a viral response lasting ≥4 years and with a histologic response of regression or arrested progression of fibrosis or inflammation.⁸ In a randomized trial of patients with chronic HCV infection, 42% of genotype 1 patients and 82% of genotype 2 or 3 patients on the pegylated regimen experienced SVR in a study of combination therapy (Table 1).¹⁶ Additionally, early HCV viral clearance is a predictor of SVR. Patients on pegylated interferon therapy show an increased phase I HCV viral clearance in comparison to patients on standard therapy. This may directly inhibit viral replication and release, resulting in a more rapid complete viral clearance as predicted by viral kinetics.¹⁹

BOX 1: Anti-HCV Drugs

Ribavirin

Ribavirin is a nucleoside analog that functions as an immunomodulator in HCV infection by influencing TNF level. Although the drug becomes incorporated into the HCV RNA, acting as a direct mutagen to the viral RNA, this is not the primary mechanism of action in the treatment of chronic infection.

Interferon alfa

Interferon alfa is a naturally occurring cytokine that the body normally produces. While it may have a minor direct antiviral effect, it functions primarily to recruit cells to kill the virus by activating resting cells. Pegylation increases the half-life of the drug.

Interferon and ribavirin are contraindicated in pregnancy.⁸

(see HCV101, page 7 for details on side effects)

BOX 2: A Measure of Prevention

According to current guidelines, vaccination against HAV is recommended for HCV-infected individuals who have no serologic evidence of immunity. Vaccination against HBV may also be beneficial as fulminant liver failure may occur following coinfection with either virus.⁶

Virus	Vaccine Brand Name, Manufacturer	Dosing schedule
HAV	HAVRIX, GlaxoSmithKline VAQTA, Merck & Co.	2 doses: 0 mo. + booster at 6-12 mo.
HBV	Engerix B, GlaxoSmithKline Recombivax HBR, Merck & Co.	3 doses: 0, 1, and 6 mo. OR 0,1, and 4 mo.
HAV/HBV	Twinrix, GlaxoSmithKline (combination vaccine)	3 doses: 0, 1, and 6 mo. ²²

Adherence is also a key component to a favorable outcome: patients who receive >80% of their doses have significantly more favorable outcome than patients who do not.^{14,15} In addition, other factors, including combination therapy, careful dosing by weight (see HCV101), age <45, female gender, and mild (rather than advanced) chronic inflammation on liver biopsy also contribute to improved treatment outcomes.

LIVER BIOPSY

Liver biopsy is necessary to assess fibrotic damage because neither HCV viral load nor ALT level correlates well with the degree of liver damage.¹⁷ There are three main indications for liver biopsy: 1) to rule out unsuspected diagnoses that may influence patient management, 2) to assess the severity of liver damage and 3) to assess response to therapy. However, the need for biopsy is a matter of debate in corrections since biopsies are both expensive and logistically complicated. Some state protocols do not require liver biopsies prior to starting treatment. Some facilities have liver biopsies provided on-site. An alternative for correctional settings is to carefully monitor response to therapy over the initial days and weeks of treatment since patients who respond immediately are believed to be likely to continue to benefit from treatment and those who do not are unlikely to benefit and might have treat-

ment discontinued (see HEPP News, April 2001).^{20,21}

HIV/HCV COINFECTION

HIV/HCV coinfection is extremely common in correctional settings. Since HIV and HCV frequently occur in the same individual and HCV exacerbates the progression of HIV, the United States Public Health Service and the Infectious Disease Society of America issued guidelines stating that HIV infected individuals should be screened for HCV²³ and named HCV an "opportunistic infection" in 1999.²⁴

Analyses of the effect of HCV and HIV coinfection on progression of either disease are often confounded by coexisting risk factors (ie IDU, EtOH) for progression. However, available data seem to indicate that HIV infection accelerates HCV liver disease causing coinfecting patients to have a shortened natural history of HCV infection.²⁵⁻²⁹ Furthermore, coinfecting patients appear to have a 12 to 300 fold higher risk of developing hepatocellular carcinoma than non-carriers.³⁰ Additionally, one study found that coinfecting patients died earlier because of their more rapid progression to cirrhosis. In this study, patients died earlier due to liver failure and not due to the development of hepatocellular carcinoma.²⁵

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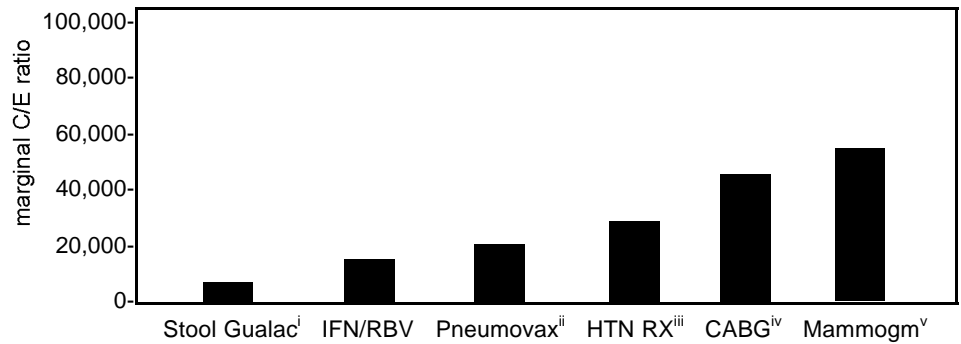
Moreover, liver inflammation can be due to ART, and this may be more frequent in those who have underlying chronic hepatitis due to HCV or HBV. It is estimated that the risk of hepatic inflammation by antiretroviral agents is approximately 4-6% in coinfecting patients.^{31, 32} Those agents that have been associated with Grade 3 or 4 transaminase abnormalities include ritonavir⁴⁴ and nevirapine. In contrast, other data have shown that those persons who were on PI containing regimens had lower fibrosis and necroinflammatory scores than those who were on non-PI containing regimens.³² Many HCV treaters would avoid ritonavir as a PI in PI doses, but agree that the small amount of ritonavir in boosted PI therapies (i.e., ritonavir/saquinavir 100/1000mg bid; ritonavir/indinavir 200/800 bid) probably poses a much smaller risk for liver inflammation in coinfecting patients. Thus, for those coinfecting persons in whom treatment has already been initiated, frequent evaluation including transaminases, total bilirubin, and CBC should be performed to monitor drug tolerance and safety. In those who are treatment naïve and HIV therapy is indicated, care should be used in choosing an initial regimen, avoiding the risk of added potential toxicity associated with certain agents.

Cellular immune response (T helper cells or CD4 T cells and Cytotoxic T lymphocytes or CD8 T cells) is involved in mounting an immune defense against HCV. During the acute phase of HCV infection, specific anti-HCV CD4 and CD8 responses are important determinants of self-limited infection.³³ Clearly, HCV infected individuals who also have advanced HIV infection (and low CD4 T cell counts) may be less able to respond to HCV infection due to their compromised cellular immune response. Therefore, in those with advanced HIV disease, it is important to treat the HIV infection first. Bringing the HIV infection under control may, in some cases, subsequently lower the HCV RNA, slowing progression of HCV-associated pathogenesis. With more CD4 cells, a patient will be more likely to mount a specific response against HCV, which will then result in a more favorable outcome for the patient. In the event that an individual is newly infected with HIV, has a good CD4 count, yet has advanced HCV infection with enough liver damage to be unable to tolerate ART, then the HCV must be treated first.

HIV/HCV RESPONSE TO THERAPY

HCV-infected and HIV/HCV coinfecting patients respond to standard interferon plus

FIGURE 3: Relative Value, Cost Effectiveness of HCV Therapy vs. Other Medical Interventions³ Wong JB. Am J Med 107(6B): 74s-78s



i. Eddy Dm. *Ann Intern Med* 1990;113:373-84; ii. Sisk JE, Riegelman RK. *Ann Intern Med* 1986;104:79-86; iii. Johannesson M. *Med Decis Making* 1994;14:236-44. iv. Tsveat J, et al. *Circulation*. 1991;83:1194-1201; v. Eddy DM. *Ann Intern Med* 1989; 111:389-99.

ribavirin HCV therapy³⁴ provided that the HIV infection of the coinfecting patient is under control, meaning that the patient's CD4 count is above 300 at the start of HCV treatment.³⁵ Studies of coinfecting patients on the new treatment standard, pegylated interferon plus ribavirin, have shown that after 12 weeks, 35% of coinfecting patients are HCV RNA negative and 43% had achieved a minimum of a 2-log reduction in HCV viral load.³⁶ A study by Turriani and colleagues has found that HIV co-infection does contribute to a slower clearance rate of HCV.³⁷ However, the discontinuation rate of coinfecting patients has matched discontinuation rates of HCV mono-infected patients (about 14 %),³⁸ indicating that HAART and HCV therapy can be concomitantly administered. Patients who start HAART early in HIV have a better clinical prognosis and decreased liver fibrosis than patients who wait to begin HIV treatment.⁴⁰

Currently, when exclusionary criteria are not present, treatment of hepatitis C is recommended for patients when CD4 and viral load values reflect good response to antiretroviral treatment. Although some controversy remains in regard to the definition of a good response to HAART, a stable CD4 T cell count greater than 300 with a stable viral load less than 400 is generally accepted.^{35, 41} Coinfecting patients should also be treated with pegylated interferon plus ribavirin, as this new standard of care results in better outcomes for coinfecting as well as HCV mono-infected patients. In a new study this treatment was well tolerated in coinfecting patients, and there were no adverse effects on the HIV disease when using pegylated interferon in combination with ribavirin.³⁵

COST OF TREATMENT

With the cost of treatment ranging between \$12,000 to \$25,000 per year per patient, the cost of treating HCV can be prohibitive to

TABLE 2: Monitoring HCV treatment

<p>Table also applies to HCV/HIV patients</p> <ul style="list-style-type: none"> ➢ Baseline <ul style="list-style-type: none"> • HIV viral load, CD4, CBC, LFTs, Chem panel, HCV load, genotype • Screen for co-morbid disease • Depression screen (consider anti-depressant prophylaxis) ➢ Week 2 <ul style="list-style-type: none"> • CBC • If anemic: erythropoietin or consider adjusting ribavirin dose ➢ 4 week intervals <ul style="list-style-type: none"> • CBC, LFTs, Chem panel • Evaluate mood, adverse effects ➢ 12 week intervals <ul style="list-style-type: none"> • HCV VL, HIV VL, CD4 • Evaluate for drug-drug interactions • Screen for IFN-associated thyroid dysfunction (TSH) ➢ Check HCV VL week 12 and 24 <ul style="list-style-type: none"> • Week 12: HCV RNA > 1 log reduction • Week 24: HCV RNA undetectable • If genotype 1, continue TX for 48 weeks. If non-genotype 1, stop therapy after 24 weeks. <p>VL (viral load); CBC (complete blood count); LFTs (liver function tests); Chem (chemistry panel); TSH (thyroid stimulating hormone).</p>

some correctional systems (see HCV101 for pricing guide). Although the treatment itself is expensive, its cost-effectiveness has been ranked in the same range as stool gualac testing, pneumococcal vaccination, and mammography (see Figure 3). Unfortunately for correctional budget managers, the cost burden falls on corrections, while the money saved by treating inmates benefits society as a whole. With rare exceptions, transplants (i.e., to replace the diseased liver with a disease-free liver) are not routinely performed on incarcerated individuals.

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HCV IN CORRECTIONS...*(continued from page 5)***MANAGEMENT**

Most experts recommend that HCV treatment be monitored by an infectious disease or GI specialist. Many HIV specialists in correctional settings have become local experts on the management of HCV, due to the high coinfection rate in their patients and because of their familiarity with the management of side effects (neutropenia, anemia) related to HCV therapy. One expert believes that "HIV caregivers who are willing to learn about hepatitis C treatment and stay current should be the ones responsible for the day-to-day care" of coinfecting patients.⁴⁵ Patients must be monitored carefully for adherence, side effects, and response to treatment. See Table 2 for suggestions for monitoring HCV treatment.

NEW GUIDELINES FOR CORRECTIONS?

The CDC and HHS have issued guidelines for the management of HIV and for HCV.⁴² These guidelines do not specifically address the management of the two viral infections in correctional settings. Due to the disproportionate prevalence of viral hepatitis among incarcerated populations, the CDC is planning to issue corrections-specific HCV management guidelines. The guidelines have been in progress since last year, and are expected to be released in late summer or early fall 2002. Although these guidelines will not suggest a specific treatment protocol, they may serve as an important reference for developing correctional standards of care and management protocols for the HCV-infected inmate. The NIH will be revising its treatment guidelines in June (see Save the Dates page 9).

CONCLUSION

When thinking about managing the HCV epidemic in corrections, it is important to keep the reality of correctional health care in perspective. If it is not possible to test all incoming inmates for HCV, savvy providers will set up protocols that will help them identify inmates who may be at high risk for HCV infection, and educate those who are not yet infected. And whereas treatment initiatives may have been poorly received in the past, armed with new data on the successful management of HIV and HCV coinfecting individuals and new data on improved outcomes due to pegylated interferon plus ribavirin, providers may be able to enroll more inmates in treatment protocols. As the CDC and the NIH compile guidelines and consensus papers this spring, correctional physicians eagerly await further direction in managing HCV and HIV/HCV co-infection among the inmate population.

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*Nothing to disclose

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- Providers must contact the Access Assurance program (1-888-437-2608) to register their patients for the first-come, first-serve wait list for PEG-Intron supply. In a written statement in January, Schering Plough estimated a 10-12 week wait for new patients beginning therapy, however the manufacturer currently does not believe anyone will have to wait the full 10-12 weeks.
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HCV IOI

HEPATITIS C TREATMENT: COMBINATION THERAPY

TREATMENT (trade name, manufacturer)	Dosing Recommendations	Cost [^]	Major side effects ^{^^}
Ribavirin: oral antiviral agent (Rebetol, Schering Plough)	Ribavirin** (200 mg capsule) ^{1, 2} : <75kg: 1000 mg given as 400 mg PO Q AM + 600 mg PO Q PM >75kg: 1200 mg given as 600 mg PO BID	Ribavirin (as unbundled Rebetol): \$9.84 per 200 mg capsule 1000 mg: \$344.40/wk 1200 mg: \$413.28/wk Rebetron (ribavirin in combination therapy*) : 1000 mg: \$402.16/wk 1200 mg: \$444.38/wk	Primary toxicity: hemolytic anemia 10%-21% (reductions of hemoglobin levels occurred within the first 1-2 weeks of therapy). Rebetron (combination therapy*): cardiac and pulmonary events associated with anaemia occurred in approximately 10% of patients. Psychiatric events in treatment naive: insomnia (39%), depression (34%), irritability (27%).
Interferon alfa-2a (Roferon A, Roche)	3 MIU 3x/week x 12 months sub-cutaneous or IM injection ⁵	\$30.60 per 3 MIU	Interferon side effects: Percentages given: pegylated / unpegylated Depression [†] : 29% / 25% Headache: 56% / 63% Fatigue: 52% / 62% Nausea: 26% / 46% Fevers: 22% / 35% Alopecia: 22% / 27%
Interferon alfa-2b (Intron A, Schering)	3 MIU 3x/week x 12 months sub-cutaneous or IM injection ³	\$40.00 per 3 MIU	
Peginterferon alfa 2b (PEG-Intron, Schering Plough) Pegasys by Roche is expected later this year	1.5 micrograms/kg/week x 12 months sub-cutaneous injection	100mcg/vial : \$247.87 160mcg/vial : \$260.27 240mcg/vial : \$273.28 300mcg/vial : \$286.93	
Interferon alfacon-1 (Infergen, Amgen)	consensus interferon 9mcg/injection.	\$38.76 per 9ug	

Monotherapy is no longer the standard of care for initial treatment.

*Rebetron is interferon alfa-2b packaged with ribavirin (Schering Plough).

**Ribavirin is FDA approved for use in combination therapy as Rebetron or with PEG-Intron as Rebetol only.

[^] All Schering prices are adjusted wholesale prices (AWP). All Roche Prices are wholesale acquisition cost (WAC). The pricing shown should be considered a maximum price. Substantially discounted pricing may be available based upon the type of pharmacy purchasing medications (ex. institutional, retail, government operated). In addition, quantity or market share rebates from the manufacturer may be available. Prices are subject to change at any time.

^{^^} Most of the reported adverse reactions are considered mild to moderate and are manageable.

[†]Note: In some larger studies, close to 70% of patients required some sort of psychiatric support while on therapy, including antidepressants. If patients begin experiencing depression while on HCV treatment, treatment with antidepressants should be initiated. Benzodiazepines should be avoided. Psychiatric support may also be appropriate in some cases.

Adapted from Chronic Hepatitis C: Current Disease Management. NIH Publication No. 99-4230, May 1999.

Additional Information from:

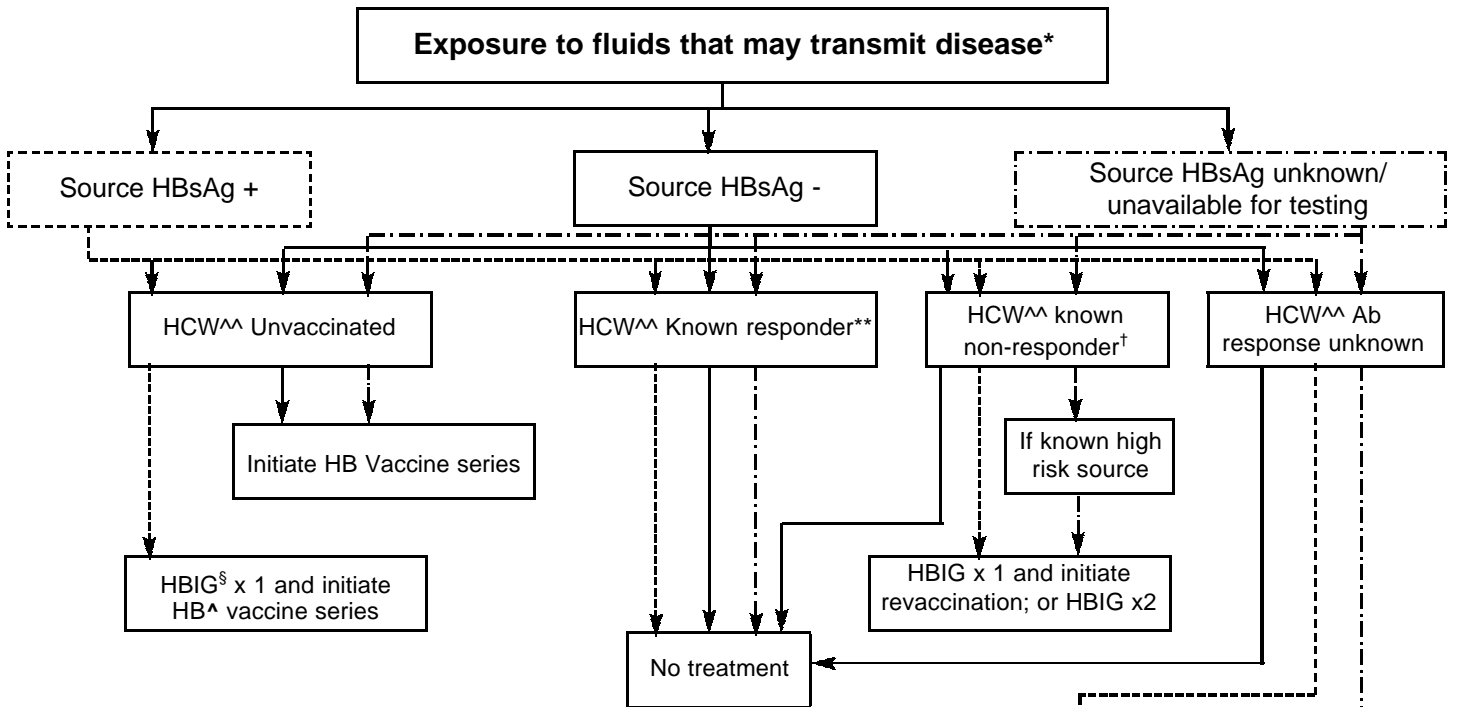
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HEPPIGRAM: Management of Hepatitis Postexposure Prophylaxis (PEP)

HEPATITIS B VIRUS (HBV) PEP



NOTES:

- Neither pregnancy nor lactation should be considered a contraindication to vaccination or treatment with HBIG.
- Persons who have previously been infected with HBV are immune to re-infection and do not require PEP.

* An exposure that may carry a risk of disease transmission is defined as a "percutaneous injury (e.g. a needlestick or cut with a sharp object) or contact of mucous membrane or non-intact skin (e.g. exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other bodily fluids that are potentially infectious."

§ Hepatitis B immune globulin; dose is 0.06 mL/kg intramuscularly; when indicated, should be given as soon as possible, preferably within 24 hours

^Hepatitis B vaccine; when indicated, should be given as soon as possible, preferably within 24 hours

^^ Health Care Worker

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

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

§§ The option of giving one dose of HBIG and reinitiating 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, 2 doses of HBG are preferred.

Test exposed person for anti-HBs^{§§}

- if adequate, no tx necessary
- if inadequate, administer HBIG x 1 and vaccine booster

Test exposed person for anti-HBs

- if adequate, no tx necessary
- if inadequate, administer vaccine booster and recheck titer in 1-2 months

HEPATITIS C VIRUS (HCV) PEP

HCV is not transmitted efficiently through exposures to blood in the occupational setting, and the incidence of anti-HCV seroconversion after accidental occupational exposure is 1.8% (0%-7%). Unlike HBV, data indicate that HCV does not survive well in the environment, suggesting that environmental contamination with blood is not a significant risk for HCV transmission in the health care setting (the only exception may be in the hemodialysis setting). In addition, there are no data supporting the use of IG (anti-HCV antibody) as PEP to prevent HCV transmission. None of the antivirals currently available to treat HCV infection are FDA approved for use in PEP, nor have any clinical trials been done to assess the effect of antivirals (ie interferon with or without ribavirin) as postexposure prophylaxis. Recommendations for postexposure management of HCV are to achieve early detection of chronic disease and, if present, refer to an expert for treatment options. There are data from studies done outside the US to suggest that a short course of interferon (IFN) alfa-2b therapy in the acute stage of HCV is associated with higher rates of resolved infection than when therapy is begun once chronic disease has been established (Jaekel E, et al. NEJM 2001; 345 (20): 1452-7). The theoretical argument exists, then, that antiviral treatment at the first signs of detectable HCV RNA may prevent the development of chronic infection.

SAVE THE DATES

Twelfth Annual Clinical Care Options for HIV Symposium

April 25-28, 2002

Miami, Florida

Sponsored by the Northwestern University School of Medicine
Visit: <http://imedoptions.com>
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Sixth Annual HIV Update: Contemporary Issues in Management

June 6-8, 2002

Boston, Massachusetts

Fee: Before April 26: \$550, \$350 Residents and Fellows; after April 26: \$595, \$375 Residents and Fellows
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Fax: 617.284.8686
Email: hms-cme@hms.harvard.edu
Continuing education credit available

Management of Hepatitis C: 2002

June 10-12, 2002

Bethesda, Maryland

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Visit: http://consensus.nih.gov/news/upcoming/hepc/hepc_info.htm
Email: hepc@prospectassoc.com
Call: 301.592.3320
Fax: 301.593.9433

XIV International AIDS Conference

July 7-12, 2002

Barcelona, Spain

Fee: before May 1: \$950; after May 1: \$1050 (special rates and scholarships available)
Visit: www.aids2002.com
Email: aids2002.registration@congrex.se

6th Annual United States Conference on AIDS (USCA)

September 19-22, 2002

Anaheim, California

Fee: before June 14th - \$330 members/ \$400 non-members; before 8/23- \$375/\$450
Visit: <http://www.nmac.org/usca2002/>
Call: Paul Woods, 202.483.6622 ext. 343
Email: pwoods@nmac.org

INSIDE NEWS

HIV

Half of HIV-positive Americans Unaware of Infection or Are Not Receiving Treatment

New York Times, 2/26/02

Data from the CDC show that nearly half of all HIV-positive Americans do not know that they are infected or are not receiving treatment for a known infection. The CDC estimates that 850,000 to 950,000 Americans are infected with HIV, with 180,000-240,000 unaware that they are infected. In addition, almost one-third of Americans who know they are HIV-positive are not receiving treatment for their disease.

Condoms in Federal Prisons Considered

AIDS Law & Policy, 17 (5); 3/15/02

In order to shift federal HIV/AIDS dollars to those hardest hit by the epidemic, a federal HIV/AIDS task force is considering condom distribution in federal prisons. This comes after an announcement by Scott Evertz (director of the White House Office of National AIDS policy) that there is going to be general shift in how federal HIV/AIDS dollars are spent. While some prison officials fear that condoms in prisons will encourage sexual behavior, other experts concentrate on the HIV epidemic behind bars as a public health issue and view condoms as a necessary part of HIV prevention.

BMS Issues Warning Regarding Stavudine

FDA website, 3/29/02; http://www.fda.gov/med-watch/SAFETY/2002/safety02.htm#zerit

Bristol-Meyers Squibb has issued a letter to health care providers warning that its antiretroviral drug stavudine (d4T, Zerit) has produced a potentially fatal neuromuscular reaction in some patients. Lactic acidosis is a potential side effect of nucleoside analogues (NRTIs), the class of drug to which stavudine belongs.

BMS warns that in these rare cases, conditions mimicking the clinical presentation of Guillain-Barre syndrome (neuromuscular weakness, respiratory problems) have resulted in the death of patients who continue to take stavudine despite lactic acidosis and other warning signs. The letter warns that health care providers should discontinue the use of stavudine by patients who develop muscle weakness. The letter is available at the above website.

Viracept Price Freeze

AP, 3/17/02

Agouron Pharmaceuticals has decided to freeze the price of its antiretroviral drug nelfinavir (Viracept) for two years. The current wholesale price is \$2.02 per tablet and the drug is taken as five tablets twice a day.

TB

Intermittent TB Therapy Resulting in Rifamycin Resistance

MMWR, 3/15/02;

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5110a5.htm

In a CDC study on rifamycin therapies in TB/HIV coinfecting patients, patients with low CD4 counts (< 60 cells/mm³) at initiation of TB therapy who received "highly intermittent regimens" (ie once- or twice-weekly therapy) tended to develop rifamycin resistance. Although more data is needed to clarify these findings, the CDC is currently recommending treating all TB/HIV coinfecting patients whose CD4 count is <100 cells/mm³ with daily TB therapy for the first two months of treatment and then with daily or three times weekly therapy for the continuation of therapy.

RESOURCES & WEBSITES

HEPATITIS RESOURCES

NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

<http://www.niddk.nih.gov>

CDC's National Center for Infectious Diseases Viral Hepatitis Page

<http://www.cdc.gov/ncidod/diseases/hepatitis/index.htm>

HepNet: Hepatitis Information Network

<http://www.hepnet.com/>

HCV/HIV CO-INFECTION RESOURCES

Update on the Management of HIV and Hepatitis C Virus Co-infection

<http://www.medscape.com/viewarticle/420681>

HCV in HIV: Challenges and Opportunities (from The PRN Notebook)

http://www.prn.org/prn_nb_cntnt/pdf/dieterich_v6n1.pdf

Conference Reports from the American Association for the Study of Liver Disease (AASLD)

<http://www.natap.org/2001/aasld2/day39.htm>

HIV RESOURCES

Three Recent HIV and Prisons Abstracts

<http://www.centerforce.org/news/index.cfm>

NEW Adult and Adolescent HIV Treatment guidelines

http://www.hivatis.org/guidelines/adult/Feb04_02/AdultGdl.pdf

NEW HHS Guidelines for the use of Antiretrovirals in Pregnant Women

http://www.hivatis.org/guidelines/perinatal/Feb4_02/Perin.pdf

HIV/AIDS Treatment Updates - Quick Reference Guide to Antiretrovirals

<http://hiv.medscape.com/Medscape/HIV/TreatmentUpdate/1998/tu01/public/toc-eng.tu01.html>

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 November 31, 2002. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. _____ is the most common type of HCV infection in the United States, with a combination treatment length of _____ weeks.
 - a) Genotype 1; 24 weeks
 - b) Non-genotype 1; 24 weeks
 - c) Genotype 1; 48 weeks
 - d) Non-Genotype 1; 48 weeks
 - e) Genotype 2; 24 weeks

2. Which of the following patients would you expect to have the greatest probability of attaining SVR on combination therapy, based on that factors that contribute to improved treatment outcomes?
 - a) male, 40, advanced chronic inflammation on biopsy, received 100% of doses
 - b) female, 35, mild chronic inflammation on biopsy, received 100% doses
 - c) female, 30, mild chronic inflammation on biopsy, received 70% of doses
 - d) male, 50, mild chronic inflammation on biopsy, received 90% doses
 - e) female, 50, advanced chronic inflammation on biopsy, received 70% of doses

3. Which of the following statement is (are) true?
 - a) HCV is considered an "opportunistic infection" in HIV infection and it is recommended that HIV-positive patients be screened for HCV infection.
 - b) A patient with a CD4 count of 400 cells/mL and a viral load of 300 copies/mL has the same probability of responding to HCV treatment as a patient who has all of the same personal characteristics but is HIV negative.
 - c) HAV and HBV vaccination are dangerous for HCV-infected individuals.
 - d) All of the above
 - e) a and b

4. For whom does HHS recommend HCV antiviral therapy? Patients who are/have:
 - a) anti-HCV positive
 - b) elevated ALT levels
 - c) detectable HCV RNA
 - d) liver biopsy that indicates fibrosis or at least moderate inflammation and necrosis
 - e) all of the above

5. The HCV/HIV coinfection rate is one-third higher in incarcerated women than in incarcerated men.
 - a) True
 - b) False

6. A 75 kg patient who meets all of the criteria for HCV therapy should be on which of the following regimens?
 - a) Ribavirin 1000 mg/day (oral) + pegylated interferon 86 micrograms/wk (injection)
 - b) Ribavirin 1000 mg/day (oral) + pegylated interferon 100 micrograms/wk (injection)
 - c) Ribavirin 1200 mg/day (oral) + pegylated interferon 112 micrograms/wk (injection)
 - d) Ribavirin 800 mg/day (oral) + pegylated interferon 117 micrograms/wk (injection)
 - e) Ribavirin 1000 mg/day (oral) + pegylated interferon 122 micrograms/wk (injection)

HEPP NEWS EVALUATION

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1. Please evaluate the following sections with respect to:

	educational value	clarity
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2. Do you feel that HEPP News helps you in your work? Why or why not?

3. What future topics should HEPP News address?

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