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HIV & Hepatitis Education Prison Project

HEPP NEWS

HIV & HEPATITIS EDUCATION PRISON PROJECT

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ABOUT HEPP

HEPP News, a forum for correctional problem solving, targets correctional administrators and HIV/AIDS and hepatitis 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 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. 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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HCV: The Correctional Conundrum

Anne S. De Groot, M.D.*, *Brown Medical School, Editor, HEPP News*

Treatment of Hepatitis C (HCV) is emerging as the most controversial subject in correctional health care. Much of the controversy around HCV testing and treatment in corrections is related to delayed recognition of the important role incarcerated individuals play in the transmission of hepatitis in the communities after they are released. State and Federal public health officials have been slow to recognize the potential benefits of screening, educating, and where possible, vaccinating incarcerated persons to prevent morbidity and mortality associated with viral hepatitis.

The Centers for Disease Control (CDC) took action this Spring, convening a meeting on Hepatitis in correctional settings that was attended by more than 100 federal and state correctional healthcare professionals.[1] Representatives of correctional organizations (ACA, NCCHC) and representatives from federal agencies such as the OSHA and NIOSH also attended the meeting. CDC speakers discussed the need to expand HBV and HCV interventions, including screening, education, vaccination, and treatment of chronic hepatitis in correctional settings. Guidelines for HCV and HBV management incorporating some of the discussion points will be issued by the CDC as a supplement to the MMWR in the Fall. While sources of funding for increased hepatitis interventions in corrections were not specifically addressed at this meeting, promoting correctional settings as outposts for public health activities may ultimately lead to increased financial support from federal and state sources for correctional treatment initiatives.

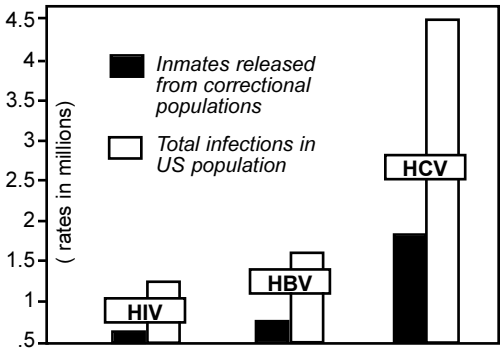
HEPP News announces a new focus on HEPATITIS.
(See Newsflashes)

In keeping with this new national focus on hepatitis in corrections, HEPP News is dedicating two of the next three issues to updates on hepatitis management. This issue addresses HCV in corrections and summarizes discussions at the CDC meeting. The second article, scheduled for June 2001, will take up the topic of Hepatitis B and Hepatitis A immunizations in correctional settings.

HCV Epidemiology

HCV and HBV outstrip HIV in terms of sheer numbers of inmates living with these two infections (Figure 1, Table 1). In the US, there are an estimated 4.5 million individuals living with chronic HCV infection, and 1.2 million with chronic HBV infection. 79% of current injection drug users have HCV infection.[3]

Figure 1. Blood Born Diseases in Corrections



Rates of blood born diseases among newly released inmates, 1996.[2]

- **Inmates At Risk**

Non hispanic blacks and hispanics have higher rates of HCV and HBV infection and chronic disease than whites; most cases of HCV and HBV infections are found among persons who are male, members of minority populations, and 30 to 49 years of age.[6] These race and class-related risk factors for hepatitis infection probably contribute to the current concentration of HCV and HBV-infected persons in prisons and jails.

According to a recent analysis by Ted Hammett for the NIJ and the NCCHC's report to Congress[7], between 1.0 to 1.25 million individuals harboring chronic HCV infection were released from prisons and jails in the U.S. in 1996, or approximately 30% (29 to 32%) of the total population living with HCV in the U.S. The prevalence of HCV infection among U.S. prisoners is at least 10 fold higher than the estimated 2% prevalence in the general population.[8]

This ratio is based on estimates that 17% of

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WHAT'S INSIDE

HCV... *(continued from page 1)*

state inmates are infected with HCV.[9] HCV infection rates have ranged from 28% (Texas) to 67% of a higher risk subpopulation of inmates (those with abnormal liver function tests or who are known to have HIV infection) in New Jersey. Reflecting their higher rate of participation in HIV and HCV risk behaviors, incarcerated women exhibit about a third higher HCV co-infection rate than incarcerated men.[10](Figure 2).

Rationale for Screening

Approximately 50% of persons with hepatitis are unaware of their hepatitis infection.[22] Testing for infection informs the patient and physician about the potential for and possible existence of liver damage. It should serve as an important prompt for a discussion about risky behaviors and transmission to others.[23] The CDC lists correctional institutions, HIV counseling and testing sites, and drug and STD treatment programs as sites where hepatitis screening and interventions should take place. (See Table 2 for recommendations.)

■ Reducing the cost of screening

If the cost of screening an incarcerated population for HCV appears to be prohibitive, targeted screening can reduce the cost of screening and still identify most HCV at-risk individuals. For example, in a Wisconsin study of HCV screening in a local prison, 60.5% of HCV infections were identified by screening those who had history of IDU. By including any individuals who also had an ALT > 51, the facility identified 79.6% of HCV infections. Adding a history of liver disease to the criteria for testing allowed the identification of 83.6% of HCV-infected individuals. When individuals who were HBV+ were also screened, the correctional facility identified 90.8% of the HCV infections. The cost of testing was reduced by two thirds (compared to mass screening) using their criteria, and was very effective.[25]

Treatment of HCV

For those who are to be treated, initial treatment of chronic HCV with ribavirin/interferon alfa is now the standard of care in community settings. Many correctional facilities are in the process of developing protocols for deciding which patients will be eligible for treatment (see the Correctional Medical Services triage form HEPPigram Part I on page 6 for an example).

■ Treatment selection criteria

Criteria for HCV treatment may vary slightly from one correctional system to another. In general, eligible patients (1) have evidence of persistent HCV infection and inflammation based on liver function test abnormalities and detectable virus in the blood stream; (2) have enough time left in their sentence to allow for completion of treatment (from six to 12 months) (3) are committed to a life free from substance and alcohol abuse; and (4) are educated about potential HCV treatment side effects and willing to adhere to an arduous course of treatment. (See HEPPigram on page 6 for guidance on selecting patients for HCV treatment.)

Table 1. Hepatitis and HIV Disease Prevalence

Hepatitis and HIV prevalence in US populations^			
	HCV	**HBV**	**HIV**
Chronic Infections	4.5 million	1.2 million	0.8 million
New Infections per year	35,000	120,000	40,000
Deaths per year	8,000	5,000	18,000
Hepatitis and HIV prevalence among inmates released from prisons and jails*			
Number of infected inmates released	1.3-1.4 million	155,000**	98,000-145,000
__% of US population	29-32%	12.4-15.5%	13-19%

^CDC, Harold Margolis, Hepatitis Branch.[4]
** Burden of disease among releasees in 1996, CDC, NIJ, Abt survey.*[5]
***Hammet et al. noted an extreme lack of HBV data on correctional populations. These numbers are rough period prevalence estimates based on studies done in California (1994) and New York (1987-1997) correctional systems.*

Figure 2. Prevalence of HCV Infection in Selected States

This figure shows the prevalence of HCV in certain state correctional populations. Percentages are shown by gender were data were available. These prevalence studies are not necessarily comparable across states because different methods were used to compile the data. HCV prevalence in reporting states is the following; ***California:*** *40% of men and 54% of women;*[11] ***Connecticut:*** *32% of women;*[12] ***Colorado:*** *30%;*[13] ***Maryland:*** *38%;*[14] ***Massachusetts:*** *20.7% (Hamden County);*[15] ***Texas:*** *28% of the men and 37% of women;*[16] ***Virginia:*** *30-40%;*[17] ***Washington:*** *30-40%;*[18] ***Wisconsin:*** *21% of women, 12.4% of men, 13.2% overall;*[19] ***Pennsylvania:*** *13%;*[20] ***Arizona:*** *31.3%.*[21]

■ Duration of treatment

Current recommendations on the duration of treatment are as follows:

Duration of Combination therapy depends on viral genotype:

–HCV genotype 2 or 3:

A 24-week (six month) course of combination therapy yields results equivalent to those of a 48-week (12 month) course.

–HCV genotype 1:

A 48-week (12 month) course yields a significantly better sustained response rate than does six months of treatment.

Duration of Interferon monotherapy: 48-weeks, regardless of genotype.

Standard therapy is to provide daily treatment with Ribavirin (usually five to six pills divided into two doses) and thrice-weekly alfa-interferon injections. (See HCV 101 on page 8 for dosing and side effects of treatment regimens). Pegylated interferon, a new form of interferon that permits once-weekly dosing, is available as PEG-Intron (peginterferon alpha-2b), and Pegasys is expected to be approved by the FDA later this Spring. Monotherapy is currently only used if the patient cannot take Ribavirin due to toxicities or side-effects.

■ Expected Response: Combination Therapy versus Monotherapy

Combination therapy consistently yields higher rates of sustained response than monotherapy. (A sustained response implies that HCV RNA remains undetectable for six months or more after therapy stops.) With combination therapy, 40% of treatment-naïve patients respond. Patients with genotype-1 have sustained response rates of 25 to 30% (slightly better response rates are seen with lower baseline HCV viral loads). Non-genotype-1 patients achieve response rates of 60 to 65%.[26,27] Other factors that increase the likelihood of a response to therapy include age <45, female gender, and mild (rather than advanced) chronic inflammation on liver biopsy. Histologic improvement occurs in 86% of patients who achieve a sustained response (SVR) and 39% of patients who relapse after initial response to combination therapy.[28] Just as with HIV therapy, adherence is critical to obtain maximal response. Adherence to therapy has also been shown to increase the likelihood of a response to therapy. The SVR increases from 40% to 48% when patients receive at least 80% of both their interferon dose and their ribavirin dose for > 80% of the recommended duration.[29]

■ Pegylated delivery: Another Step Forward in Hepatitis C Therapy

Pegylated forms of interferon allow once

Continued on page 4

Letter from the Editor

Dear Colleagues,

As our experience with highly active antiretroviral therapy and long-term survival expands, we now manage co-morbid diseases that never had time to manifest in the past, such as Hepatitis C (HCV). HCV infection contributes to the deaths of an estimated 8,000 - 10,000 Americans each year. This toll is expected to triple by the year 2010 and exceed the number of annual deaths due to AIDS, according to the CDC.

Hepatitis C infection shares many of the epidemiologic risk factors associated with HIV. Indeed, coinfection rates in the HIV+ population average 30-35%, but can be as high as 100% in specific settings. Thus, testing for the co-related virus is a must in order to provide early intervention and evaluation, as well as begin risk reduction counseling and training.

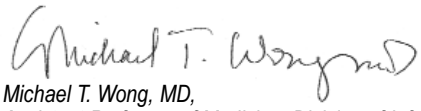
Treatment options for both viruses are also unclear. Some HIV antiretrovirals appear to have a greater risk for hepatotoxicity than others, independently of HCV infection. The treatment balance lies in the ability to effectively evaluate the HCV infection with not only viral load, genotype and imaging, but also with liver biopsy as chemical hepatitis often does not correlate with the degree of liver injury present.

As with many other chronic medical conditions, morbidity and/or mortality attributable to HCV may not manifest itself until well after the end of incarceration. Consequently, correctional systems, when faced with the dilemma of prioritizing treatment for HCV, may choose to spend the funds otherwise, or not at all. Much of the controversy is related to the cost of a therapy that is difficult to administer and, in many cases, ineffective. Additionally, the therapy in most cases is being given to IDUs who are in forced institutional abstinence, have not and will not have drug treatment, and will therefore probably be promptly reinfected upon release.

Despite these concerns, some state medical directors have lead the way and adopted clear protocols for the screening and treatment of HCV in their facilities. These visionaries are mindful that a year 2001 dollar spent on treatment may reduce the cost (to society) of caring for patients who may require liver transplants in 20 to 30 years. Furthermore, combination therapy of HCV is leading to higher rates of cure (up to 88% in selected patients), therefore, the overall cost effectiveness of HCV interventions in corrections is improving. Obviously, more data are needed to more concretely guide our treatment programs. Until then, we can only continue to do the best with what information we have.

After reviewing this issue, readers should be able to describe the rationale for HCV testing and treatment, review the interactions between HCV and HIV, describe the risk of HCV infection for inmates and correctional workers, and provide preliminary information on new formulations of therapy. Thank you for your continued support of HEPP News!

Sincerely,



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HCV... *(continued from page 2)*

weekly dosing, improving adherence to therapy and possibly improving response to therapy. A phase III study demonstrated that the combination of peginterferon alfa-2b (1.5 mcg/kg once weekly) plus ribavirin was significantly more effective than the combination of standard interferon alfa-2b plus ribavirin, particularly in patients with genotype 1 virus.[30, 31] SVR rates in this study were dependent on the actual dose received. Overall, patients who received >10.6 mg/kg/daily of ribavirin plus 1.5 mcg/kg/QW of peginterferon alfa-2b achieved a SVR of 61%. The SVR in genotype 1 patients was 48% and the SVR in non-genotype 1 patients was 88%.[32]

This study also demonstrated that these response rates could be further increased if patients were able to maintain adherence. Regardless of genotype, patients who received the recommended combination regimen and received >80% of their treatment had a higher sustained response than those who received < 80% of their treatment (72% vs. 46%). Genotype 1 patients who received the optimal weight-based dose of peginterferon alfa-2b plus ribavirin and adhered to at least 80% of their regimen achieved a SVR of 63%. Similar patients with genotype 2 or 3 infection achieved a SVR of 94%.[33, 34]

■ **Liver Biopsy**

The need for confirming the extent of damage to the liver by HCV and chronic HBV infection is another area of debate, since obtaining liver biopsies can be both costly and logistically complicated in correctional settings. Liver function tests can be normal in patients with rather advanced cirrhotic features. Likewise, liver function tests may be consistently elevated in Hepatitis C patients with normal histology. Some state correctional systems do not routinely perform liver biopsies prior to initiating treatment, because of cost and logistical difficulties. Other states (e.g. FL) feel biopsies are the only real way to measure disease progression over time and therefore have made arrangement to do them on site at very reduced costs ($200 per biopsy). Depending on the cost of obtaining a liver biopsy, electing to treat all incarcerated individuals who meet the criteria for treatment may be more cost-effective, for society as a whole, than management by biopsy.[35]

■ **Lowest cost intervention: Education**

The lowest cost intervention for the prevention of hepatitis infection is education. Given the risk of acquiring HCV (not to mention HIV), all bloodborne pathogen screening events should lead to careful discussion of the risks of acquiring HBV and HCV infection (for those patients who have negative hepatitis serologies). The risk of transmitting hepatitis should also be made very clear (see Resources on page 9 for educational materials).

The impact of continued drug use should also be made very clear to patients, especially those who are not yet HCV infected.

Table 2. HCV / HBV Screening

Persons who should be tested routinely for hepatitis include:

- Persons residing in correctional facilities
- IDU, including those who injected once or a few times and do not currently consider themselves to be drug users.
- Persons with selected medical conditions, including:·
  - Persons who received clotting factor concentrates produced before 1987
  - Persons ever on chronic hemodialysis;
  - Persons with persistently abnormal ALT levels.
- Persons who received blood transfusions, blood components, or organ transplantation before July 1992
- Persons diagnosed with HIV infection and sexual partners of persons diagnosed with HIV infection
- Healthcare and correctional workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood.

Source: Modified from MMWR, 1998[24]

Young injection drug users (IDUs) acquire HCV infection at rates four times higher than the rate of acquisition of HIV; after 5 years of injection drug use, 90% of IDUs are HCV infected. For those inmates already infected with HCV, education should be provided on the impact of alcohol abuse on HCV progression (four fold increase in risk of progression, risk of liver damage directly correlated with alcohol intake) and the risk of transmission to uninfected sexual partners. Inmates who have HCV infection should, at the very least, be educated about options for treatment even if they are not eligible for treatment while incarcerated (see Resources on page 9 for expanded access programs).

■ **Additional considerations**

Another lower (but not no-cost) intervention is vaccination. For HCV infected patients, vaccination against HBV and HAV is routinely recommended, as these relatively inexpensive vaccines may reduce the risk of fulminant liver failure and the need for liver transplantation for HCV-infected patients. A new schedule of HBV vaccination (three shots at 0, 1, and 4 months) has received approval. The first shot provides up to 50% protection, and the series does have efficacy even if prolonged over several years, so the new CDC guidelines are expected to encourage HBV vaccination even in jail settings.

Should patients be ineligible for treatment due to lack of time to complete the treatment, they should be provided with the hotline numbers to access free HCV treatments, if eligible, after release. Contact the companies for more information on their expanded access programs (see Newsflashes page 9).

Cost of HCV treatment

With the high prevalence of HCV infection among incarcerated individuals, there is a concern that treatment could overwhelm some systems' healthcare budgets. Medical decision analyst J. Wong calculated that six months of combination therapy resulted in net savings in the range of $400 to $3500 over the lifetime of each HCV infected patient.[36] Dr. Wong's analysis ranked combination therapy for HCV in the same range of cost effectiveness as stool guiac testing, pneumococcal vaccination, coronary bypass surgery, and mammography. It must be noted however that the cost savings that may accrue from treatment of prisoners are primarily to society as a whole. While treatment of incarcerated individuals for hepatitis and HIV is the right thing to do and can tremendously benefit the public health, it is not realistic to expect correctional systems to shoulder this financial burden without assistance.

Table 3. Monitoring HCV Treatment

Table also applies to HCV/HIV patients

- Baseline

-HIV viral load, CD4, CBC, LFTs, Chem panel, HCV load, genotype
-Screen for co-morbid disease
-Depression screen (consider anti-depressant prophylaxis)

- Week 2

-CBC
-If anemic; erythropoeitin

- 4 week intervals

-CBC, LFTs, Chem panel
-Evaluate mood, adverse effects

- 12 week intervals

-HCV VL, HIV VL, CD4
-Evaluate for drug-drug interactions
-Screen for IFN-associated thyroid dysfunction (TSH)

- Check HCV VL week 12 and 24

-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.

VL (viral load); CBC (complete blood count); LFTs (liver function tests); Chem (chemistry panel); TSH (thyroid stimulating hormone).

■ **Management**

Since the incidence of side effects to HCV combination therapy can be relatively high, and it can be difficult for incarcerated patients to quickly access their clinician to report side effects, it is important to:
–spend time preparing the patient for the potential treatment-related side effects,
–consider following the patients in a dedicated hepatitis clinic,

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HCV... *(continued from page 4)*

–use a nurse or other staff person to regularly check in with patients who are receiving HCV treatment so that side effects can be rapidly addressed.

One suggestion for reducing the cost of managing chronically HCV infected individuals in corrections is to make use of existing "chronic disease" clinic infrastructure and expertise existing on site - since HIV and HCV are fellow travelers, and correctional medical units might insist that the ID (HIV) expert acquire expertise in HCV and HBV management. Some clinics have set up flow sheets to reduce repetitive, unnecessary testing.

Without a good support system, a high percentage of patients will fail to complete therapy. Because of the high cost of treatment, time spent preparing patients and supporting them while on treatment is likely to be cost effective.

HIV and HCV co-infection

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 the virus. Clearly, HCV infected individuals who also have advanced HIV infection may be less able to respond to HCV infection due to their compromised cellular immune response.

Analyses of the effect of HCV and HIV co-infection on progression of either disease are often confounded by concurrent risk factors for progression. However, available data seems to indicate that HIV infection accelerates HCV liver disease. Persons who are co-infected (HIV / HCV) appear to have a 12 to 300 fold higher risk of developing hepatocellular carcinoma than non-carriers.[37] Furthermore, antiretroviral agents can contribute to liver inflammation, and this may be more frequent in those who have underlying chronic hepatitis due to HCV or HBV. Ritonavir appears to be one of the ART medications that is most commonly associated with liver inflammation in HCV/HIV co-infected patients.[38]

The impact of HCV infection on HIV infection is less clear. In some studies, HCV infection does not appear to have an effect on the progression of HIV.[39] Other studies have reported an association between more rapid progression to AIDS or death in HIV-infected patients; particularly among those who were co-infected with HCV genotypes 1a and 1b.[40, 41] However, a report by Sulkowski at CROI contraindicated these findings, suggesting that risk of progression was more linked to lack of access to medical care (for HIV) in his cohort of African American patients who had HIV and HCV co-infection (CROI abstract 34).

Response to HCV therapy in individuals who also have HIV infection appears to be equivalent to that of non-HIV infected individuals.[42] A recent study in the Journal of the American Medical Association by Sulkowski et al indicates that 88% of co-infected patients tolerate concurrent HCV treatment and HAART.[43] Following successful HCV treatment, co-infected patients are not more likely to relapse after HCV treatment than are patients who do not have concurrent HIV infection.

Currently, when exclusionary criteria are not present (see Table 2), 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 200 with a stable viral load less than 400 is generally accepted.[44]

Conclusion

In summary, the high prevalence of hepatitis infections among incarcerated individuals and the availability of treatments with less than 100% efficacy forces difficult decision making in correctional health facilities. Combination IFN/ribavirin therapy is now the standard of care. National guidelines and standards for selecting patients who are to be treated, while providing access to care for HCV infected individuals regardless of incarceration status, are forthcoming from the CDC. The cost of HCV treatment is expected to be a major barrier to wide implementation of the guidelines in prisons and jails. Correctional physicians eagerly anticipate further guidance from state and federal health officials on supplemental sources of funding for HCV treatment initiatives in correctional settings.

** Consultant & Speaker's Bureau: Agouron Pharmaceuticals, Dupont, Merck, Roche, Boehringer-Ingelheim/Roxane Laboratories*

REFERENCES:

1. CDC consultants' meeting, Recommendations for Prevention and Control of Viral Hepatitis in Correctional Settings. March 5-7th 2001, Crowne Plaza Ravinia Hotel, Atlanta GA)
2. Hammett TM, Harmon P, and Rhodes W. The Burden of Infectious Disease Among Inmates and Releasees from Correctional Facilities. Prepared for National Commission on Correctional Health Care- National Institute of Justice "Health of Soon-to-be-Released Inmates" Project, June 14-15, 1999, Chicago IL. 25.
3. CDC. MMWR. October 16, 1998 / 47(RR19);1-39.
4. Harold Margolis, Hepatitis Branch NCID, CDC. Prevention and Control of Viral Hepatitis in the Community. CDC Consultants' Meeting, 2001.
5. Hammett et al, 1999.
6. CDC. MMWR. October 16, 1998 / 47(RR19);1-39
7. Hammett et al, 1999.
8. Hepatitis Control Report, Winter 1999-2000; 4(4), 1.
9. Hammett et al, 1999.
10. Reindollar RW. Am J Med, 1999 Dec 27; 107(6B): 100S-103S.
11. Ruiz JD, Molitor F, Sun RK et al. West J Med. 1999 Mar; 170(3): 156-60.
12. Fennie KP, Selwyn PA, Altice FL. Poster abstract TU.C.2655 presented at the XI International Conference on AIDS, Vancouver, July 9, 1996.
13. Spaulding A. Prev Med 1999 January: 28(1); 92-100.
14. Vlahov D, Nelson KE, Quinn TC, Kendig N. European J Epidemiology 1993 September; 9: 566-9.
15. Conklin T, et al. Draft presented at Recommendations for Prevention and Control of Viral Hepatitis in Correctional Settings; CDC Consultants' Meeting, Atlanta GA, March 5-7, 2001.
16. Hepatitis C control in prison remains an elusive goal. Hepatitis Control Report, Winter 1999-2000; 4(4), 1.
17. Richmond-Time Dispatch Online 5/3/99.
18. Schueler L. Presentation at Symposium on Current Strategies for the Treatment and Prevention of HIV in Corrections, Sponsored by Brown University AIDS Program and Yale University HIV in Prisons Porgram, New York City, October 24, 1998.
19. Pfister JR. Recommendations for Prevention and Control of Viral Hepatitis in Correctional Settings; CDC Consultants' Meeting, Atlanta GA, March 5-7, 2001.
20. Maue, F. Recommendations for Prevention and Control of Viral Hepatitis in Correctional Settings; CDC Consultants' Meeting, Atlanta GA, March 5-7, 2001.
21. Gerard Chamberlin, MPH, Arizona Department of Corrections Health Services 2005 N Central # 700 Phoenix, AZ 85004 (602) 255-4222. Personal communication, 4/01.
22. Hammett et al, 1999.
23. See the CDC Serostatus Approach to Fighting the Epidemic, SAFE, March issue of HEPP News.
24. Modified from "Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease." MMWR October 16, 1998:47(RR19);1-39
25. Pfister et al. 2001.
26. Poynard T, Marcellin P, Lee SS et al. Lancet. 1998; 352:1426-1432.
27. Serfaty L, Aumaitre H, Chazouilleres O, et al. Hepatology, 1998; 27: 1435-1440.
28. Ibid.
29. McHutchison JG, et al. Hepatology. 2000;32:223A.)
30. Schiff ER, Maddrey WC, et al. Tx Reporter. Jan 2001; 7-9.
31. Mans MP, McHutchinson JG, Gordon S, et al.
32. Manns MP, McHutchison JG, Gordon S, et al. [abstract 552]. Hepatology 2000;32:297A.
33. Schiff ER, Maddrey WC, et al. Tx Reporter. Jan 2001; 7-9.
34. Manns MP, McHutchison JG, Gordon S, et al. [abstract 552]. Hepatology 2000;32:297A.
35. Wong JB. Am J Med. 2000 Apr 1; 10895): 366-73.)
36. Ibid.
37. National Institutes of Health Consensus Development Conference Panel Statement: Management of Hepatitis C. Hepatology 1997; 26 (Suppl 1): 2S-10S.
38. Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. JAMA 2000 Jan 5;283(1):74-80.
39. Staples CT, Rimland D, Dudas D. CID 1999; 29: 150-4
40. Sabin, CA, Telfer P, Phillips AN, Bhagani S., Lee CA. J Infec Dis 1997, 175: 164-168.
41. Soriano V, Rodriguez-Rosaldo R, Garcia-Samaniego J. AIDS 1999, 13 (5):539-546.
42. Soriano V, Garcia-Samaniego J, Bravo R, et al. Clin Infect Dis 1996, 23:585-591.
43. Sulkowski et al, 2000.
44. Carpenter CJ, Cooper DA, Fischl MA, et al. JAMA 2000, January 19; 283(3): 381-391.

HEPPigram Part I: Management and Treatment of Chronic HCV

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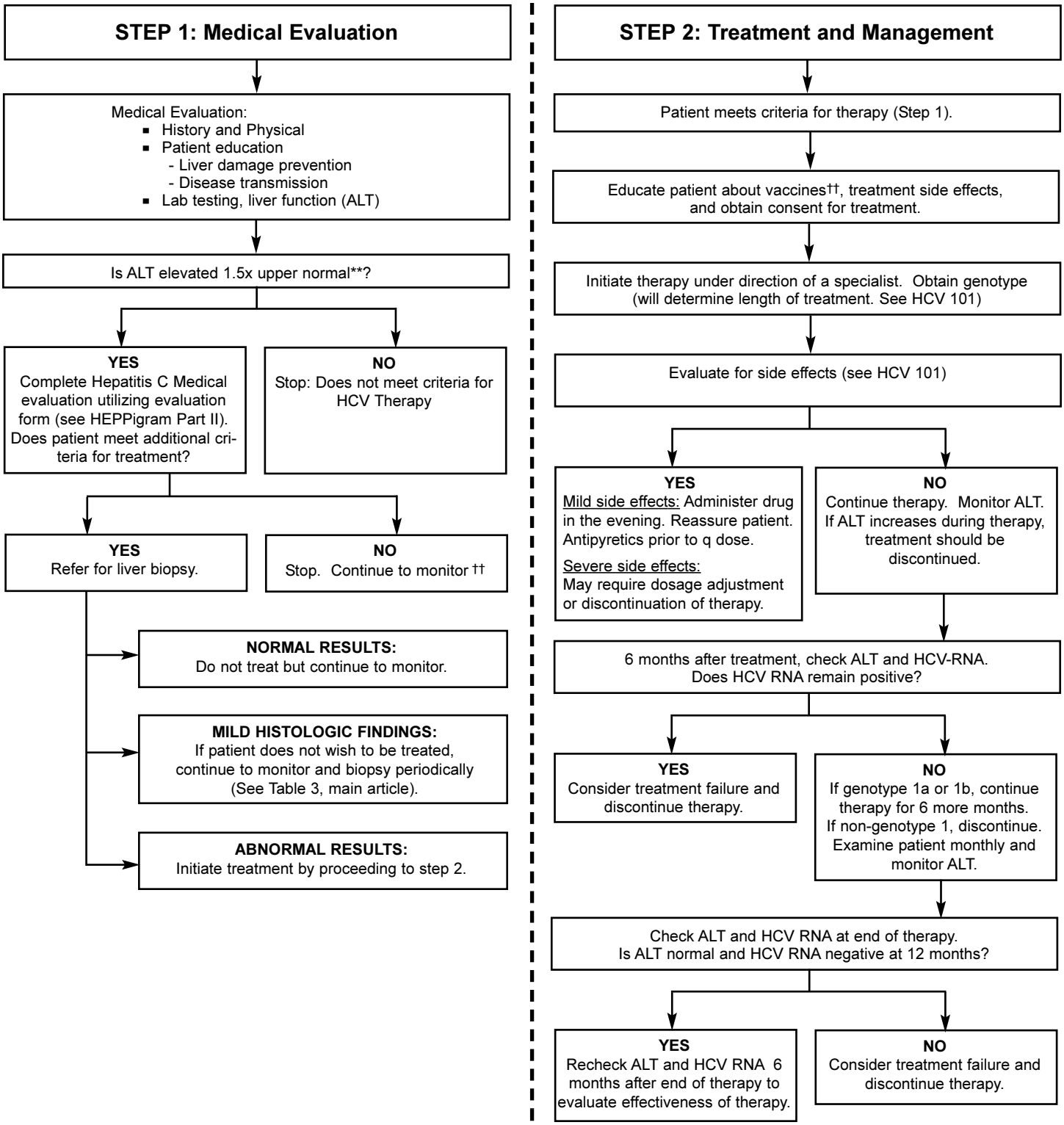

*** Different institutions may use different criteria for eligibility*

†† Hepatitis A and Hepatitis B vaccination are recommended if immunity is not already established.

HEPPIGRAM PART II: One Approach to Hepatitis C Medical Evaluation

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RATIONALE	OBJECTIVE	FINDINGS
Screen for HCV Infection if risk factors (blood products before 1990 or IDU in patient with increased ALT), no confirmatory test needed.	Positive HCV-EIA?	⬭Yes ⬭No
Confirm chronic hepatitis elevated ALT (three tests, >1 month apart over previous 12 months, average >1.5 x upper normal).	#1 ALT _____ date _____ #2 ALT _____ date _____ #3 ALT _____ date _____ Average >1.5x upper normal?	⬭Yes ⬭No
No evidence of treatment benefit if under age 18 or over 60 years of age	Age____ Age >18 and <60?	⬭Yes ⬭No
Treatment for HCV is lengthy with significant side effects.	Has patient received education regarding length of therapy, possible side effects, and expected outcomes and consents to therapy?	⬭Yes ⬭No
Ribavirin causes birth defects.	Willing to use contraception if released during treatment and for 6 mos post treatment? Woman HCG negative?	⬭Yes ⬭No ⬭Yes ⬭No
Heavy ethanol use or injecting drug use will eliminate HCV treatment benefit.	Free of substance abuse misconduct guilty findings for previous 12 months? Consents to random drug testing?	⬭Yes ⬭No ⬭Yes ⬭No
HCV progresses slowly and therapy is problematic; treatment must be completed while incarcerated. If not able to complete treatment courses during incarceration, treatment should be deferred until release.	Maximum release date:_____ Maximum release date in >18 months?	⬭Yes ⬭No
Hepatitis C treatment is arduous, which makes patient adherence and compliance mandatory.	History of non-compliance to medical therapy and/or follow-up?	⬭Yes ⬭No
Interferon worsens hyperthyroidism.	TSH: _____ Results indicate hyperthyroidism?	⬭Yes ⬭No
Interferon worsens autoimmune disease: SLE, rheumatoid arthritis, MCTD, Scleroderma, etc.	Convincing evidence of autoimmune disease? ANA: _____	⬭Yes ⬭No
Interferon causes solid organ transplant rejection.	History of solid organ transplant?	⬭Yes ⬭No
Interferon reduces platelets, especially in the first 4-6 weeks.	Platelet count: _____ Platelets <100,000?	⬭Yes ⬭No
Interferon in combination with ribavirin will decrease Hbg 2.5-3.1 in 4-6 weeks.	Hbg: _____ Hbg within normal limits?	⬭Yes ⬭No
Interferon in combination with ribavirin will reduce WBC's.	WBC: _____ WBC's within normal limits (>3,000cells/cubic ml)?	⬭Yes ⬭No
Interferon therapy in combination with ribavirin may exacerbate cerebrovascular disease.	Does patient have a history of cerebrovascular disease?	⬭Yes ⬭No
Interferon therapy in combination with ribavirin may exacerbate heart failure.	Does patient have history of coronary artery disease or heart failure?	⬭Yes ⬭No
Interferon therapy in combination with ribavirin can cause renal failure.	Is serum creatinine stable at <2.0?	⬭Yes ⬭No
There is no evidence of therapy benefits in patients with decompensated cirrhosis. There is little evidence of benefit and very low sustained response in patients with compensated cirrhosis.	Variceal bleed past/present? Encephalopathy past/present? Evidence of ascities? Albumin: _____ Albumin <3.0? PT: _____ PT >14? Alpha fetoprotein:_____ AFP>50? Total bilirubin/conj bilirubin:_____ Is patient jaundiced?	⬭Yes ⬭No ⬭Yes ⬭No ⬭Yes ⬭No ⬭Yes ⬭No ⬭Yes ⬭No ⬭Yes ⬭No ⬭Yes ⬭No
Interferon may cause or exacerbate major depression.	History of major depression or suicide ideation? History of major psychiatric illness?	⬭Yes ⬭No ⬭Yes ⬭No
Co-infection of HIV and HCV requires that HIV be controlled.	HIV Ab positive? HIV Ab:_____? Date: _____ If HIV positive: CD4: _____ Viral load: _____	⬭Yes ⬭No
Co-infection with HBV and HCV may require higher doses of interferon.	HbsAg: _____	⬭Yes ⬭No

HCV 101

Hepatitis C Treatment

TREATMENT (Trade Name)	COST^ (Manufacturer)	DOSE	FREQUENCY	MAJOR SIDE EFFECTS^^
Combination Therapy				
Ribavirin: oral antiviral agent**+	Ribavirin: $1.25 per 200mg capsule 1000mg: $43.75/week 1200mg: $52.50/week See below for interferons. Rebetron** 1200 (Schering-Plough): $391.00 per week Rebetron** 1000: $354.00 per week Rebetron 600: $290.00 per week	Ribavirin: 200mg capsules (1000mg/day divided BID or <75kg; 1,200mg/day divided BID for >75kg)	2x day	Primary toxicity: hemolytic anemia (reductions of hemoglobin levels occurred within the first 1-2 weeks of therapy).
Interferon alfa-2a, interferon alfa-2b, consensus interferon		Interferons: 3 million units (MU) /injection; consensus interferon 9 mcg/injection.	3x week sub-cutaneous	Rebetron: cardiac and pulmonary events associated with anemia occur in approximately 10% of patients. Psychiatric events in treatment naive: insomnia (39%), depression (34%), irritability (27%).
Monotherapy				
Interferon alfa-2a (Roferon A)	$36.72 per 3MU (Roche)	3 MU/injection	3x weekly sub-cutaneous	Most patients experience flu-like symptoms: headache, dizziness,nausea/vomiting, diarrhea, depression, irritability, insomnia. Some patients experience: Neutropenia, Thrombocytopenia, Depression, Anemia
Interferon alfa-2b (Intron A)	$40.00 per 3 MU (Schering-Plough)	3 MU/injection	3x weekly sub-cutaneous	
Peginterferon alfa 2b (PEG-Intron. Pegasys by Roche is expected later this year)	100mcg/ml : $240.00 160mcg/ml : $253.00 240mcg/ml: $265.00 300mcg.ml : $279.00 (Schering-Plough)	Monotherapy: 1mcg/kg per weekCombination therapy: 1.5mcg/kg per week	1x weekly	
Interferon alfacon-1 (Infergen)	$38.76 per 9ug(Amgen)	consensus interferon 9 mcg/injection.	3x weekly	

**Reserve for patients who have contraindications to Ribavirin.*
***Currently, Ribavirin is only available from Schering-Plough packaged with Interferon alfa-2b as Rebetron or compounded by Fisher's Pharmacy (3904 Perrysville Ave., Pittsburgh, PA 15214; 888-347-3416). Rebetron contains Interferon 3 MU plus 1200mg, 1000mg, or 600mg Ribavirin, and is packaged in 2 week supplies.*
^ 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.

DETAILS ARE IN TEXT
Adapted from Chronic Hepatitis C: Current Disease Management. NIH Publication No. 99-4230, May 1999. www.niddk.nih.gov.

CME is Now Available Online at www.hivcorrections.org:

HEPP readers are now able to take HEPP News' continuing medical education (CME) tests online at http://www.HIVcorrections.org. Any internet browser will enable you to take the HEPP News CME tests every month. Your test results will be registered with the Brown Medical School Office for Continuing Medical Education. When you pass the test, you can either download your CME certificate from the website or request Brown to send the certificate in the mail. Try it out this week!

Save the Dates

National Hepatitis Awareness Month
May 2001
For details, see Hepatitis Foundation International, http://www.hepfi.org.

Infectious Disease Society of America (IDSA): 39th Annual Meeting
October 25-28, 2001
San Francisco, California
Abstract deadline: May 22, 2001
Late-breaker abstract deadline: August 20, 2001
Discounted registration deadline: July 30, 2001
Write: 99 Canal Center Plaza, Suite 210 Alexandria, VA 22314
Fax: 703.299.0204
Visit: www.idsociety.org

The 5th Annual HIV Update: Contemporary Issues in Management
May 31-June 2, 2001
Cambridge, Massachusetts
Email: hms-cme@hms.harvard.edu
Visit: http://134.174.17.108/conted-bin/hmscme
Call: 617.432.1525
Fax: 617.432.1562
Fee: $530/full fee; $340/residents and fellows in training; $340/non-physician fee. Continuing medical education credits are available.

Management of HIV/ AIDS in the Correctional Setting: A Live Satellite Videoconference Series "Management of the HIV/ Hepatitis C Co-infected Patient"
June 5, 2001
12:30-3:30 p.m. EST
CME Credits Available through Albany Medical Center.
Call: 518.262.4674
Email: rosentjh@mail.amc.edu
Visit: www.amc.edu/patient/HIV/hivconf.htm

Overview of Adult HIV Care for Health Professionals
June 4-6, 2001
Atlanta, Georgia
Email: pyeargi@emory.edu
Visit: http://www.seatec.emory.edu
Call: 404.727.2938
Fax: 404.727.4562
Fee: $150, includes book, syllabus material, and optional clinical rotation. Continuing education credits available.

News Flashes

HEPP News includes new focus on Hepatitis
Almost one third of our nation's Hepatitis C cases occur among recently released prison and jail inmates. For this reason, HEPP News has expanded its focus to include topics on Hepatitis C. Our new name is the HIV and Hepatitis Education Prison Project (our acronym will remain the same: HEPP).

We are happy to announce new members of our advisory board, Dr. Dean Rieger, Medical Director of the Indiana Department of Corrections, and Dr. Josiah Rich, Associate Professor of Medicine and Community Health, Brown University School of Medicine, and Attending Physician at The Miriam Hospital.

We would also like to acknowledge our financial supporters for the year 2001, and thank those that funded us last year. Renewing their annual support, HEPP News is grateful for the unrestricted educational grants from Abbott Laboratories, Agouron Pharmaceuticals, Boehringer-Ingelheim/Roxane Laboratories, DuPont Pharmaceuticals, Merck & Co. , and Roche Pharmaceuticals. Schering-Plough Corporations has joined our supporters. In addition, OrthoBiotech has contributed baseline support.

Hepatitis C Rising in Arizona State Prisons
Hepatitis C (HCV) is on the rise in Arizona state prisons. While an estimated 1.4 million HCV-infected prisoners spend time in the nation's jail system each year, Arizona estimates that approximately 6,000 of its 26,800 inmates are infected with the disease. Prison doctors estimate that between 700 and 1,000 are eligible for treatment; however, who will pay for that treatment is causing controversy. Treating HCV would cost the Arizona Department of Corrections between $8,700 and $16,200 per eligible inmate. (Madrid D. Denver Post. 2/17/01 P. A28. www.denverpost.com)

Hidden Behind Bars: Hepatitis C
Hepatitis C in prisons has picked up attention from the Reuters News Service, a backbone for the general press. An April 5 Reuters report included commentary from HEPP News editor Anne De Groot, Ted Hammett of Abt Associates and HEPP News Advisor, and various national HCV and HIV prison experts. The article calls Hepatitis C "a silent killer" and reported that medical experts say HCV is not only rampant among the almost two million inmates of U.S. prisons and jails, but authorities are not making enough effort to combat it. Reuters interviewed Hammett about a study he conducted for the Texas prison system which concluded it would cost $40 million a year to diagnose and treat prisoners for hepatitis C in that state. The complete story is available at www.reuters.com or by calling the Washington newsroom 202-898-8300.

New Releases: Pegylated Interferon
Schering-Plough has received FDA approval for use of Peginterferon alfa-2b (PEG-Intron) in monotherapy, and is expecting approval for use with Ribavirin later this year. Peginterferon alfa-2b is a longer-acting form of interferon alfa-2b (Intron A) that is a once-weekly therapy designed to optimize the balance between antiviral activity and elimination half-life. Roche Laboratories is also expecting approval for their peginterferon alfa-2b, known as Pegasys. Both companies have reimbursement plans for their Hepatitis C medications. For Schering-Plough, call Commitment to Care at 1-800-521-7151 (9:00am-8pm). For Roche's reimbursement plan, call the Hepline Reimbursement Hotline 800-443-6676, option 3 (8:30am-5:00pm). For more information, call Schering-Plough at (908) 298-4000 or visit http://www.pegintron.com, and call Roche at 800-526-6367 or visit: http://www.rocheusa.com.

Resources

The Price of Punishment
Hepatitis C in prisons. A WBUR interview with A. De Groot and J. Noonan.
http://www.wbur.org/prison/hepatitis.shtml

Combination Therapy
Projects in Knowledge (slide sets and CME materials supported by an unrestricted grant from Schering Oncology/Biotech)
http://www.projectsinknowledge.com/HepC-DDW/home.htm

Hepatitis C Awareness News is a free educational newsletter. Staff and inmates can subscribe by writing to: Hepatitis C Awareness Project, PO Box 41803, Eugene, OR 97404.

HEPATITIS WEBSITES:

CDC hepatitis home page
http://www.cdc.gov/ncidod/diseases/hepatitis/index.htm

NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
http://www.niddk.nih.gov

HIV and Hepatitis C Co-Infection: ATIS
http://www.hivatis.org/hepatitisC.html

American Liver Foundation
http://www.liverfoundation.org

Canadian Hepatitis information website
http://www.hepnet.com/index.html

HCV Advocate: News and information website on HCV and HIV/HCV coinfection
http://www.hcvadvocate.org

HCV Prison News: A new website dedicated to hepatitis C and HIV/HCV coinfection in prisons
http://hcvprisonnews.org

Self-Assessment Test for Continuing Medical Education Credit

Brown Medical School designates this educational activity for 1 hour in category 1 credit for Bloodborne Pathogens Universal Precautions and 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 August 31, 2001. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Which of the following indicate the correct schedule(s) for HBV vaccine?
   a) ~~0~~, 6, 12 months
   b) ~~0~~, 1, 4 months
   c) 0, 2, 6 months
   d) 0, 3, 6 months
   e) a and b
   f) b and c

2. A patient infected with HCV genotype 2 who is eligible for treatment can expect which duration for treatment?
   a) 16-week (4 month) course of combination therapy
   b) 24-week (6 month) course of combination therapy
   c) 48-week (12 month) course of combination therapy
   d) 6-12 months of therapy; depending on weather LFTs show response to treatment.

3. At what point should you consider treatment failure and discontinue therapy?
   a) After initiating therapy if patient presents severe side effects.
   b) At 6 months, if HCV RNA remains positive.
   c) At 12 months, if HCV RNA remains positive.
   d) All of the above
   e) None of the above; treatment success cannot be measured until after therapy is complete.

4. Which of the following statements are false?
   a) Persons being treated for HCV should use contraception during treatment and for 6 months post treatment because ribavirin can cause birth defects.
   b) Interferon in combination with ribavirin can exacerbate cerebrovascular disease and heart failure, and can cause renal failure.
   c) Treatment for HCV is lengthy with significant side effects, therefore should not be initiated in the correctional setting.
   d) Monotherapy should only be used for patients who have contraindications for ribavirin.
   e) a and b.
   f) b and c.

5. Indicate which of the following statements are true about HCV and HIV coinfection:
   a) Persons who are co-infected (HIV/HCV) appear to have a 12 to 300 fold higher risk of developing hepatocellular carcinoma than non-carriers.
   b) HIV infection accelerates HCV liver disease.
   c) A majority of patients can tolerate concurrent treatment for HCV and HIV.
   d) a and b.
   e) All of the Above.
   f) None of the above.

6. Approximately ___ of US HCV infections occur in people released from prisons or jails:
   a) 2%
   b) 11%
   c) 24%
   d) 30%
   e) 50%

HEPP News Evaluation

5 Excellent 4 Very Good 3 Fair 2 Poor 1 Very Poor

1. Please evaluate the following sections with respect to:

	educational value	clarity
Main Article	5 4 3 2 1	5 4 3 2 1
HEPPigram	5 4 3 2 1	5 4 3 2 1
HCV 101	5 4 3 2 1	5 4 3 2 1
Save the Dates	5 4 3 2 1	5 4 3 2 1

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

3. What future topics should HEPP News address?

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

5. Do you have specific comments on this issue?

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