THEBODY PRO
The HIV/AIDS Resource for Healthcare Professionals

E-mail a colleague

SEARCH: GO

HIV JournalView

Margaret Hoffman-Terry, M.D.

by Margaret Hoffman-Terry, M.D., F.A.C.P., A.A.H.I.V.S.
Clinical Associate Professor of Medicine, Penn State University College of Medicine

from The Body Pro

May/June 2005

Table of Contents

- From Crumbling Joints to Clotting Blood Vessels, Studies of the Aquitaine Cohort Examine Factors Associated With Avascular Necrosis and Atherosclerosis
  - Avascular Necrosis and HIV/HAART
  - Changes in Atherosclerosis Progression in HIV
  - Recommended Reading on Cardiovascular Disease in HIV
- Long-Term Tenofovir Use May Be Associated With Mild Nephrotoxicity
- CNS Symptoms From Efavirenz Not Always Time-Limited
- In the World of Hepatitis C Treatment, It's All About Teamwork
- Footnotes

From Crumbling Joints to Clotting Blood Vessels, Studies of the Aquitaine Cohort Examine Factors Associated With Avascular Necrosis and Atherosclerosis

With the "graying" of the HIV population and survival now measured in decades rather than years, metabolic syndromes have rapidly moved to the forefront as causes of morbidity and mortality. Large cohort studies, such as the two discussed below on avascular necrosis and atherosclerosis, continue to supply pieces of the puzzle as to exactly why these syndromes occur, which patients are at greatest risk, what the root causes are and what we can do to impact their progression.

Avascular Necrosis and HIV/HAART

Lawson-Ayayi S, Bonnet F, Bernardin E, et al, for the Groupe d'Epidémiologie Clinique du SIDA en Aquitaine (GECSA). *Avascular necrosis in HIV-infected patients: a case-control study from the Aquitaine Cohort, 1997-2002, France****. Clin Infect Dis. April 15, 2005;40(8):1188-1193.***

The Aquitaine Cohort comprises patients prospectively enrolled since 1987 in a hospital-based surveillance system of HIV infection in southwestern France. The system uses a standardized reporting form that is completed for each patient every 3 to 6 months at each physician contact or in the case of an intercurrent event.

The risk of avascular necrosis is 45 times greater in an HIV-infected person as compared to in the general population, suggesting either HIV itself or the treatment of HIV as causal.[1,2] A case-control study of the Aquitaine Cohort by François Dabis and Patrick Mercié for the French Groupe d'Epidémiologie Clinique du SIDA en Aquitaine (GECSA) sought to examine this issue.

All symptomatic cases of avascular necrosis reported from 1997 to 2002 were investigated. A

nested case-control model was used, with each of the 12 radiologically confirmed cases matched to 3 controls from the same cohort on the basis of age and years since HIV diagnosis, CD4+ cell count at the time of HIV diagnosis and duration of follow-up after HIV diagnosis.

Two multivariate models were developed: one looked at the association of avascular necrosis with demographic, clinical and laboratory data and the second looked at drug treatment history. Eleven of the 12 cases were men, 9 of the 12 cases carried the diagnosis of AIDS, the median time since HIV diagnosis was 10.4 years, and all had been on at least 3 antiretrovirals, including a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI).

When all identified risk factors from the 2 models were combined in the final model, only current heavy alcohol intake or steroid use -- even short-courses -- were strongly associated with the occurrence of avascular necrosis (adjusted odds ratio [aOR] 16.96, *P* = .04).

Fat accumulation, which previously has been thought to be associated with avascular necrosis, had an aOR of 22.67, but an insignificant *P* value of .08. Of significance, antiretroviral therapy, including PIs, was *not* associated with avascular necrosis. The majority of cases and controls had received antiretroviral therapy from the French national healthcare system, which provides easy access to HIV treatment.

The Bottom Line

This is the first detailed analysis of the relationship between specific antiretroviral therapies and avascular necrosis, and the first to rule out an association. Intriguing data to be sure, except rather than changing our antiretroviral therapy-prescribing habits, it leads us instead to recommend that alcohol and steroid use be limited in order to prevent avascular necrosis.

However, a number of important caveats accompany this study:

1. only symptomatic cases of avascular necrosis were examined,
2. the number of cases is relatively small, and
3. the providers assessed alcohol intake, but extrapolation to other populations may be difficult since average daily alcohol intake by the French may be greater than that in other countries.

Large collaborative epidemiological studies are still needed to corroborate these important findings.

Changes in Atherosclerosis Progression in HIV

Thiebaut R, Aurillac-Lavignolle V, Bonnet F, et al, and the Groupe d'Epidémiologie Clinique du SIDA en Aquitaine (GECSA). *Change in atherosclerosis progression in HIV-infected patients: ANRS Aquitaine Cohort, 1999-2004****. AIDS. April 29, 2005;19(7):729-731.***

Soon after highly active antiretroviral therapy (HAART) became available, case reports began appearing that pointed to an increased risk of cardiovascular disease. Large cohort studies, such as Mary-Krause's French Hospital Database, have since confirmed this increased risk.[3]

With studies showing increased intima-media thickness (IMT) in HAART-treated patients, primarily among those with traditional risk factors for cardiovascular disease, since 2000 international guidelines have recommended practices aimed at reducing this risk, such as the use of lipid-lowering drugs and non-PI regimens when possible. François Dabis, Patrick Mercié, et al conducted another study of the Aquitaine Cohort, this time looking at IMT. The study examined 233 Aquitaine Cohort patients followed from 1999 to 2004 who had their carotid IMT measured over a 36-month time period as a marker of cardiovascular disease risk. This was the same time period during which interventions to reduce the risk of cardiovascular disease became commonplace in French medical practice, thus providing a unique opportunity to examine the impact of such interventions.

Patients included here were from the SUPRA study, which also looked at carotid IMT in a subset of patients drawn from the Aquitaine cohort (a large cohort followed prospectively via database and trials in France). The SUPRA study was published in 2002, so these investigators examined

patients prior to the initiation of the recommended interventions to reduce cardiovascular risk.[4] Carotid IMT was measured by B-mode ultrasonography at baseline and at months 12 and 36 of follow-up, with information on risk factors for cardiovascular disease collected, in addition to the usual cohort data.

The median baseline age of the cohort was 44, 25% were women, 59% were smokers, 32% had been diagnosed with AIDS and 55% were on PI-based HAART. During the first 12 months, while 63 of the patients benefited from at least one intervention to lower cardiovascular disease (lipid-lowering drugs, non-PI-based HAART and smoking cessation), lipid profiles remained stable and carotid IMT increased from 0.55 to 0.57 mm (P<.0001).

By the end of the 36 months of follow-up, 17% of the cohort were receiving lipid-lowering drugs, 60% were on a non-PI-based regimen (40% were on a PI-based regimen) and 49% were non-smokers (51% were smokers). From month 12 to month 36 of the follow-up, there was a significant decrease in total and low-density lipoprotein (LDL) cholesterol, and median carotid IMT decreased from 0.57 to 0.53 mm (P<.0001). While the proportion of patients exercising at least once a week was 30% throughout the study and body mass index remained stable at 22.6, the percentage of patients who exercised more than once a week increased. Having analyzed the possible associations at the individual level between IMT evolution and interventions reducing cardiovascular disease, the only significant association with a lifestyle intervention was with smoking cessation (P = .06).

The Bottom Line

Although the study was non-randomized, relatively small and may have been limited by the increased vigilance towards improving cardiovascular health (on the part of both providers and patients who had access to the baseline IMT results and cardiovascular risk assessment), the improvement in carotid IMT -- which is a surrogate marker of long-term atherosclerosis -- and the association with smoking cessation are important. Bogged down in the day to day hectic routine of clinical practice, providers often forget to make sure that their patients are following the three key, and inexpensive, steps to improved health: diet, exercise and smoking cessation. The full impact lipid-lowering drugs, non-PI HAART and smoking cessation will have on the clinical endpoints of cardiovascular disease remains to be proven by large collaborative studies, but in the meantime, smoking cessation is definitely a good first step.

Recommended Reading on Cardiovascular Disease in HIV

Kamin DS, Grinspoon SK. Cardiovascular disease in HIV-positive patients. AIDS. April 29, 2005;19(7):641-652.

The April 29, 2005 issue of AIDS contains an outstanding review of cardiovascular disease in HIV-infected patients by two experts in the field: Daniel Kamin and Steven Grinspoon from Massachusetts General Hospital. Covered topics range from risk factors to biochemical markers of disease to outcome models to treatment. A thorough review and well worth the read.

Long-Term Tenofovir Use May Be Associated With Mild Nephrotoxicity

Gallant JE, Parish MA, Keruly JC, Moore RD. *Changes in renal function associated with tenofovir disoproxil fumarate treatment, compared with nucleoside reverse-transcriptase inhibitor treatment****. Clin Infect Dis. April 15, 2005;40(8):1194-1198.***

Renal disease remains an ongoing concern in an HIV population increasingly at risk by virtue of advancing age, the increasing prevalence of ethnic and racial groups that are pre-disposed to renal disease, such as African-Americans, and the use of antiretroviral drugs that come to market without long-term safety studies on end-organ damage.

Joel Gallant and Richard Moore from The Johns Hopkins University School of Medicine examined renal function in a large observational cohort of patients looking for degree of and factors associated with renal dysfunction. Those of us who have been in HIV practice since before the new millennium remember adefovir dipivoxil (Hepsera) as the first nucleotide reverse transcriptase inhibitor (NtRTI) to reach the expanded access stage for HIV. Now marketed at lower doses for hepatitis B suppression, it never was approved for HIV because of high rates of renal dysfunction at the dose needed to treat HIV.[5] While its cousin tenofovir (TDF, Viread) has an excellent renal

safety profile in the 144-week data from Gilead's 903 trial, the potential for renal dysfunction has remained in many practitioners' minds.[6] While most case reports have been of patients with underlying systemic or renal disease, some reports have been of patients with no identifiable risk factors. From a pharmacological standpoint, it is known that tenofovir co-administration with drugs which are eliminated by active tubular secretion or drugs that decrease renal function may result in increased tenofovir levels.

The investigators analyzed all patients in the Hopkins HIV clinical cohort database who were starting a HAART regimen containing tenofovir or a nucleoside reverse transcriptase inhibitor (NsRTI) between January 1, 2001 and December 31, 2003. Creatinine clearance was calculated via the Cockcroft-Gault equation, using an average of the two values collected closest to initiation of therapy, one year after therapy initiation, and the maximum creatinine value reached during therapy. Three hundred forty-four patients received tenofovir and 314 received an NsRTI.

The groups were similar, with the following exceptions: greater use of lopinavir/ritonavir (LPV/r, Kaletra) in the tenofovir group and greater use of efavirenz (EFV, Sustiva, Stocrin) in the NsRTI group. Compared to the NsRTI group, the tenofovir group had significantly greater increases in serum creatinine levels (+0.15 mg/dL versus +0.10, with $P = .01$) and decreases in absolute (-13.3 mL/min versus -7.5, with $P = .005$) and percentage creatinine clearance (-10% versus -6%, with $P = .007$).

There was no difference in the rate of treatment discontinuation coincident with maximum decline in creatinine clearance. In multivariate analysis, only tenofovir use ($P = .006$) and a CD4+ cell count below 50 cells/cc ($P<.001$) were associated with a decline in creatinine clearance. A baseline creatinine clearance below 50 mL/min and diabetes were less strongly associated ($P = .10$). Hypertension status, use of lopinavir/ritonavir or other antiretroviral agents, HIV-1 RNA viral load, previous use of adefovir dipivoxil, age, sex, ethnicity, and HIV transmission risk factor were *not* associated with a decline in creatinine clearance.

The Bottom Line

While tenofovir was not associated with nephrotoxicity in clinical trials, trial patients are a select group and may not represent the real world of clinical practice. The relative decline in creatinine clearance associated with the use of tenofovir was 4% compared to NsRTIs. Urinalysis and serum phosphates were not routinely performed, so the incidence of proteinuria or Fanconi's syndrome could not be determined. Emerging differences in creatinine clearance may be a function of time, as initial analysis of this cohort showed no significant differences at 246 days of follow-up compared to the 322 for the current analysis. Thus, the take-home is that over time, providers should be aware of a possible modest decline in renal function in tenofovir-treated patients, especially patients with advanced immunosuppression, diabetes or baseline decreased renal function. While only time will tell the full story behind this question and the authors don't recommend withholding tenofovir from patients who would benefit from it, "constant vigilance" (for Harry Potter fans, that's a direct quote from Mad-Eye Moody) is the key.

CNS Symptoms From Efavirenz Not Always Time-Limited

Fumaz CR, Munoz-Moreno JA, Molto J, et al. *Long-term neuropsychiatric disorders on efavirenz-based approaches: quality of life, psychologic issues, and adherence****. J Acquir Immune Defic Syndr. April 15, 2005;38(5):560-565.***

Although efavirenz has been known to cause neuropsychiatric disturbances, studies to date have focused on the majority of patients for whom these symptoms are self-limited, rather than on the minority for whom they may continue unabated for months to years. Because efavirenz is the preferred NNRTI for first-line regimens recommended by the Department of Health and Human Services' treatment guidelines,[7] its frequent use is likely to continue. While its one-pill once-a-day dosing makes it attractive from an adherence standpoint, potential adherence barriers, such as ongoing neuropsychiatric symptoms, need to be examined.

This cross-sectional comparative study from Bonaventura Clotet's group in Barcelona, Spain, interviewed 120 patients who had been receiving a stable efavirenz or a PI-based regimen for at least one year. Patients had to be over 18 years of age, free of concurrent opportunistic infections or acute illnesses and have no history of depression, schizophrenia or other psychotic or personality disorders. All efavirenz patients were directed to take their medication at bedtime, with efavirenz levels drawn between 0800 and 0900.

Quality of life was assessed with the Medical Outcomes Study (MOS)-HIV questionnaire, which provides information on multiple dimensions of health, ranging from pain to social functioning to quality of life. Psychological status was evaluated with the Profile of Mood State (POMS-A), which has 15 questions measuring the 5 affective states of depression, vigor, anger, tension and fatigue, resulting in a total mood score ranging from -12 to 48. Higher scores indicated greater mood disturbance. Other psychological variables were assessed using a 10-point visual analogue scale, including effort to follow treatment schedule, self-efficacy, and limitations as a result of adverse events, health beliefs and worry/limitation associated with lipodystrophy.

The investigators recruited 120 patients, with no significant sociodemographic or clinical characteristic differences between arms. PI patients had been on the same regimen for a longer time (P = .004) and had a higher CD4+ cell count (P =.02) than the efavirenz group. The percentage of patients who had a CD4+ cell count of less than 200 was similar. The most used PI was nelfinavir (NFV, Viracept).

Fifty-four percent of patients in the efavirenz group and 27% in the PI group reported at least one neuropsychiatric disorder within a month prior to the visit (P = .002). The efavirenz group reported a statistically significantly higher prevalence of dizziness, sadness, mood changes, irritability, lightheadedness, nervousness, impaired concentration, abnormal dreams and somnolence. Mean efavirenz levels were not significantly different between subjects with and without neuropsychiatric symptoms and high plasma levels of efavirenz were not associated with symptoms.

There were no significant differences between groups regarding quality of life. The median POMS-A score was 4 in the efavirenz group and 3 in the PI group (P = .09) with no differences on any of the subscales. Comparison with regard to the other psychological variables was not different between groups.

Sixty percent of efavirenz patients and 55% of PI patients reported more than 95% adherence. In univariate analysis, age, lack of substance abuse and effort to follow the treatment schedule were associated with adherence. An inverse relationship between time on treatment and adherence was observed, with adherence decreasing over time on treatment. In multivariate analysis, only lack of substance abuse and effort to follow the treatment schedule were predictors of adherence more than 95%.

The Bottom Line

While over half of the efavirenz patients had persistent neuropsychiatric symptoms on long-term therapy (mean of 91.1 weeks on an efavirenz-based regimen), these symptoms were usually mild and clinically tolerable. More than half of the patients were employed and able to maintain an active life. As has been reported in past studies, abnormal dreams, sadness, irritability, nervousness, lightheadedness and difficulty in sleeping were the most frequent adverse events in the efavirenz group, with the statistically significant increase in these symptoms in the efavirenz group, leading the investigators to surmise that this drug was playing a key role.

While previous researchers have found a correlation between high efavirenz levels and central nervous system (CNS) symptoms, none was found here, perhaps because patients who had high levels had already discontinued therapy due to the symptoms.[8] An important caveat to this study is that patients who had mental health histories that included depression were excluded from participating. Thus these results may not be reflective of the full range of patients for whom this drug is prescribed. However, the persistence of symptoms at almost 2 years of follow-up in over half of the efavirenz patients is a key finding and one that bears remembering in day-to-day clinical practice.

In the World of Hepatitis C Treatment, It's All About Teamwork

Fleming CA, Tumilty S, Murray JE, Nunes D. *Challenges in the treatment of patients coinfected with HIV and hepatitis C virus: need for team care****. Clin Infect Dis. April 15, 2005;40(Suppl 5): S349-S354.***

The April 15, 2005 supplement to Clinical Infectious Diseases contains many articles worth reading, but one of the most useful articles for the provider treating or considering treating hepatitis C (HCV) in patients with HIV, is Catherine Fleming's article regarding her group's experience in setting up an HCV coinfection treatment clinic for the over 1,000 HIV-infected patients followed at Boston Medical Center.

With over 50% of their HIV-infected patients coinfected with HCV and over 50% of deaths in their HIV-infected patients attributable to HCV, Fleming et al felt a compelling need to open a clinic devoted to evaluating and treating HCV in this population. Since January of 2000, this clinic has been staffed by a multidisciplinary team that includes a hepatologist, an infectious disease specialist, a psychiatrist, a dedicated nurse and substance abuse counselors.

A study was conducted in February of 2002, with a review of all charts to assess interferon treatment eligibility, subsequent start of treatment, and outcome if treatment commenced. In addition to the coinfection clinic cohort, the Hepatitis and AIDS Liver Outcomes (HALO) Study was established at Boston Medical Center in August of 2000 to prospectively evaluate the natural history of HIV and HCV in an inner city population. Approximately 80% of the coinfection clinic are enrolled in this study with a detailed patient questionnaire, physical and chart review performed at baseline and then yearly in follow-up. Demographics of the HALO patients closely resemble those of the general coinfection clinic population.

To date, 260 coinfection clinic patients and 274 HALO patients have been evaluated, representing less than 50% of the HIV/HCV coinfected patients believed to be receiving their primary care at Boston Medical Center. The HALO patient demographics in themselves tell the story of why HCV treatment in the HIV population is fraught with difficulties.

At study entry:

- 42% of the trial participants had less than a high school education
- 36% were homeless
- 22% were employed for pay
- 82% were current or past heroin users
- 48% had used injection drugs within the past 6 months
- 24% had ongoing alcohol abuse

In terms of concurrent morbidity:

- 43% were receiving treatment for ongoing psychiatric disease
- 23% had a CD4+ cell count of less than 200 cells/cc
- 7% had advanced liver disease as indicated by a Child-Pugh class >7

Of the 149 patients completing assessment in the coinfection clinic, only 30% were eligible for treatment. Factors leading to classification as ineligible were:

- nonadherence with appointments (23%)
- ongoing injection drug use or alcohol abuse (23%)
- active psychiatric disease (21%)
- advanced HIV disease (13%)
- decompensated liver disease (12%)
- severe comorbid medical illness (8%)

Sixty-four percent of the 44 patients who were eligible for treatment were not treated because of their reluctance to embark on a course of treatment. Some of the reasons patients gave for their decision not to be treated included, unstable social circumstances, fear of potential adverse effects

of the treatment, concern about their ability to work while on treatment and fear of potential relapse of intravenous drug use when required to self-inject HIV meds.

Six patients didn't return after discussing treatment and 3 relocated, highlighting the difficulty of establishing long-term intervention in this group. Interestingly, non-genotype 1 patients were more likely to commence treatment than genotype 1 patients (53% versus 26% of eligible patients), suggesting that the *perception* of effectiveness of treatment may contribute to overcoming patient reluctance to start therapy.

In the coinfection clinic, each patient was assumed to have only 1 condition rendering them ineligible for treatment. In the HALO cohort, the issue of multiple coexistent barriers to treatment was examined. Only 12% of patients were found eligible by standard screening criteria. Thirty-four percent had 2 conditions rendering them ineligible and 22% had 3 or more such conditions. These results highlight the interrelationships between drug and alcohol abuse, psychiatric disease, clinic non-attendance and poor social supports and the need to evaluate all medical and social issues in these patients. To date, 21 coinfection clinic patients have begun HCV therapy, which represents only 8% of the 260 patients referred.

Treatment statistics are as follows:

- Four patients are currently undergoing therapy.
- Eight patients have completed therapy.
- Nine patients discontinued treatment prematurely: 4 discontinued due to acute psychiatric problems, 4 discontinued because of medical complications (refractory anemia, lactic acidosis, pneumonitis and retinal hemorrhage) and 1 was lost to follow-up. Four of the patients who discontinued prematurely relapsed into intravenous drug use.

Of the 8 patients who completed therapy:

- Five were non-responders.
- One patient had an end-of-treatment response (this usually refers to someone who has an undetectable HCV viral load at the end of his/her 48 weeks of HCV therapy, but the disease then recurs and after treatment is stopped the HCV viral load rises, meaning that ultimately they weren't cured).
- Two achieved sustained virologic response (both non-genotype 1).

Overall, there was a treatment success rate of less than 1% for patients referred to the coinfection clinic.

There are many challenges to the access of HCV care by the HIV-infected population: Many providers don't screen or refer patients appropriately. Even when referred, patients' lack of insurance can be a huge barrier -- since not only are the HCV antivirals costly and often obtainable only after a lengthy prior authorization process or thru compassionate need pharmaceutical programs, but the adjunctive medications, such as hematopoietic growth factors, that are required in order to complete a full course of therapy are often difficult to obtain.

While U.S. National Institutes of Health guidelines recommend screening active intravenous drug users and considering treatment for them on a case by case basis, limited data on treating this population exists. The possibility of HCV reinfection with recurrent intravenous drug use remains a grim specter that also must be addressed.

Other issues with this population include hazardous drinking, which 20% of this cohort met the definition of. As has been noted, alcohol adversely affects treatment response, thus abstinence during treatment is recommended.[9-10]

Another issue often seen with this population is psychiatric illness. A successful course of HCV therapy would ideally require pretreatment of psychiatric illnesses with close follow-up. Many coinfected patients are anemic or leukopenic from their HIV or other concomitant illnesses. If their anemia and leucopenia are treated with injectable hematopoietic growth factors like epogen or neupogen *prior* to starting their interferon and ribavirin (Copegus, Rebetol, Virazole) -- both of

which usually worsen anemia and leukopenia -- you can usually get patients thru the required 48 weeks of treatment.

In addition, while no studies exist on overcoming patients' fears of treatment with interferon, the authors (and I) believe education is the key, as many patients will accept therapy after ongoing education.

The investigators emphasize that supporting patients through treatment is the crucial cog in the wheel. Pretreatment with selective serotonin reuptake inhibitors may help prevent the common symptoms of anxiety/depression that develop in 50% of patients on treatment.

Hematopoietic growth factors, such as erythropoietin and G-CSF, should be used aggressively for the anemia and leukopenia that frequently develop during HCV therapy.

Advising patients ahead of time that their absolute CD4+ cell count will likely drop on therapy, but that their CD4 percentage will stay the same, and that no increased risk of opportunistic infections has been seen to date (i.e., in trials such as APRICOT,[11] which followed 800+ coinfected patients on interferon and ribavirin and tracked their CD4s, with no increase in opportunistic infections seen during that study), can be an important intervention -- otherwise, in this author's experience, patients' intense fear of advancing HIV infection may result in their premature discontinuation of HCV therapy.

The investigators also note the importance of monitoring for thyroid abnormalities and exacerbation of autoimmune disease. Pancreatitis, lactic acidosis and weight loss are all possibilities while on therapy for HCV. They note that prescribing didanosine (ddI, Videx) in conjunction with ribavirin should be avoided because of the increased risk of lactic acidosis and decompensated liver disease when these two drugs are used concomitantly (as per data from the APRICOT[11] trial). Also, lactate levels should be frequently checked in patients with new/increasing symptoms of myalgias, dyspnea, edema, etc.

Nutritional support to help ameliorate the average 4.6 kg weight loss during a course of HCV therapy can also be key.

Boston Medical Center is looking at educating referring providers about the need to refer patients early (13% of the patients that were referred to Boston Medical College already had decompensated liver disease). In addition, the investigators suggest that the referral process should be revised so that all coinfected patients are automatically referred.

Another suggestion was the implementation of an educational session with a nurse early in the course of evaluation to teach patients about HCV therapy. In addition, substance abuse and social issues should be evaluated, with ongoing access to case managers, substance abuse counselors and education sessions.

To deal with psychiatric issues, they note it would be beneficial to have a dedicated psychiatrist to evaluate and follow all patients with active psychiatric issues (many experienced HCV treaters would advocate for evaluation of *all* treatment candidates, not just those identified as having mental health problems).

Other suggestions include the implementation of reminder calls for appointments and the addition of a Spanish-speaking provider to better serve that population. Directly observed therapy for pegylated interferon, especially in the intravenous drug user population, is a consideration.

The Bottom Line

The treatment of HCV in the HIV population, as outlined in this article, is a difficult, although not insurmountable, challenge. If we look at the multi-pronged approach to successful HIV treatment that has developed over the course of decades and we apply the lessons learned to the treatment of HCV, we can look to overall treatment success rates closer to the 30% to 40% seen in studies such as the APRICOT trial.[11]

With HCV we can use the "C" word and talk about a cure, something we can't do with HIV. Given the fact that HCV is now the number one cause of death for HIV-infected patients in many HIV clinics around the country, if we are to have any hope of stemming the rising tide of HCV-related

deaths, the time for watchful waiting is over. We need to implement successful treatment programs for all HIV-infected patients with chronic active HCV.

Footnotes

1. Brown P, Crane L. Avascular necrosis of bone in patients with human immunodeficiency virus infection: report of 6 cases and review of the literature. Clin Infect Dis. April 15, 2001;32(8):1221-1226.

2. Monier P, McKown K, Bronze MS. Osteonecrosis complicating highly active antiretroviral therapy in patients infected with human immunodeficiency virus. Clin Infect Dis. December 2000;31(6):1488-1492.

3. Mary-Krause M, Cotte L, Simon A, Partisani M, Costagliola D, and the Clinical Epidemiology Group from the French Hospital Database. Increased risk of myocardial infarction with duration of protease inhibitor therapy in HIV-infected men. AIDS. November 21, 2003;17 (17):2479-2486.

4. Mercié P, Thiébaut R, Lavignolle V, et al. Evaluation of cardiovascular risk factors in HIV-1 infected patients using carotid intima media thickness measurement. Ann Med. January 1, 2002;34(1):55-63.

5. Benhamou Y, Bochet M, Thibault V, et al. Safety and efficacy of adefovir dipivoxil in patients co-infected with HIV -1 and lamivudine resistant hepatitis B virus: an open-label pilot study. Lancet. September 1, 2001;358(9283):718-723.

6. Staszewski S, Gallant JE, Pozniak AL, et al. Three-year analysis of the renal safety of tenofovir DF (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in antiretroviral-naive patients. In: Program and abstracts of the XV International AIDS Conference; July 11-16, 2004; Bangkok, Thailand. Abstract WePeB5917.

7. Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. US Dept of Health and Human Services; April 7, 2005.

8. Marzolini C, Telenti A, Decosterd LA, Greub G, Biollaz J, Buclin T. Efavirenz plasma levels can predict treatment failure and central nervous system side effects in HIV-1-infected patients. AIDS. January 5, 2001;15(1):71-75.

9. Schiff ER. Hepatitis C and alcohol. Hepatology. September 1997;26(3 Suppl 1):39S-42S.

10. Bhattacharya R, Shuhart MC. Hepatitis C and alcohol: interactions, outcomes, and implications. J Clin Gastroenterology. March 2003;36(3):242-252.

11. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, et al, for the APRICOT Study Group. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. New Engl J Med. July 29, 2004;351(5):438-450.

Please fill out this quick survey and tell us what you think of this HIV JournalView article!

For a complete index of The Body Pro's HIV JournalViews, click here.

Please note: Knowledge about HIV changes rapidly. Note the date of this article, and before treating patients or employing any therapies described in these materials, verify all information independently. If you are a patient, please consult a doctor or other medical professional before

acting on any of the information presented in this article.

© 2005 Body Health Resources Corporation