

Consider Prognosis in HIV With Comorbidities

Clinicians need to decide which comorbidities are worth worrying about in the HIV-positive population.

BY HEIDI SPLETE
Senior Writer

WASHINGTON — More HIV patients are living long enough to die of non-HIV causes, and clinicians who treat these patients will need to juggle the management of HIV with the management of other medical conditions, said Dr. Amy C. Justice at the Ryan White CARE Act meeting on HIV treatment.

"It's not appropriate to take guidelines for patients who don't have HIV and blindly apply them to people with a very different prognosis," said Dr. Justice, of the West Haven Veteran's Affairs Medical Center and Yale University, both in New Haven, Conn.

Adapting guidelines intended for general populations to HIV patients remains a challenge, Dr. Justice acknowledged. Patients with HIV are a special population that is more likely to drink heavily, smoke, have viral hepatitis, and have some type of mental illness. In addition, many HIV patients are poor and have few resources, she said.

However, the same demographic factors—including age, race, and sex—that influence the development of comorbidities in the general population also apply to HIV patients.

The bottom line is that clinicians need to decide which comorbidities are worth worrying about in the HIV-positive popu-

lation. Dr. Justice advises clinicians to consider three questions:

► What is the prognosis? Will the HIV patient live long enough to benefit from treatment for a comorbid condition?

► What is the impact on the patient and his or her community? Is the condition prevalent and harmful?

► What is the benefit of intervention? Even if a condition is prevalent and harmful (such as diabetes), treating it may not improve the patient's outcome.

Although antiviral therapy has extended the life expectancy of HIV patients, data have shown that the survival rate drops with age. Based on census data and a computer simulation developed at Yale University, more HIV patients are likely to die from non-HIV causes than from HIV in the future.

"The older you are, the more likely you are to die a non-AIDS-related death because you have increasing rates of comorbid illness as you get older," Dr. Justice explained. If the mean age at HIV diagnosis remains 38 years, the mean age at death will likely approach 58 years before long, she added.

Hepatitis C, hypertension, diabetes, and chronic obstructive pulmonary disease are the most common comorbidities among HIV patients, with prevalences of 34%, 32%, 13%, and 12%, respectively, according to data from the Veterans Aging Cohort 3 Site Study (VACS3).

The study, conducted by Dr. Justice and her colleagues, involved a review of the records of more than 800 HIV-positive patients seen at veterans' hospitals between June 1999 and July 2000 (*Med. Care* 2006;44:S52-60).

"Theoretically, HIV itself may alter the association between the condition and the outcome," Dr. Justice said. For example, HIV may make diabetes worse. The stress of fighting the virus may affect the body's blood glucose levels, in the same way that active bacterial infections do. Comorbidities also

have an impact on survival rates in HIV patients through their effects on antiviral therapy adherence, she said.

For example, substance use may not only reduce adherence to HIV treatment, but it may also exacerbate comorbid conditions.

Alcohol is the substance most commonly used by HIV patients, Dr. Justice said. Data from multiple studies have shown that 60%-75% of patients with HIV infection drink alcohol, 40%-50% use tobacco, and 30% use other drugs such as marijuana, cocaine, and heroin.

"The level of alcohol use that may be harmful in HIV patients may be substantially lower than the level that is harmful in non-HIV patients," Dr. Justice noted. Alcohol use by HIV patients makes the treatment of hepatitis C and

other illnesses more difficult. "And it certainly increases the possibility of risky sex and poor adherence to medication," she said.

Also, the detrimental effects of smoking may be exacerbated in HIV patients; studies suggest that HIV patients who smoke are at increased risk for emphysema, lung cancer, pneumonia, heart disease, and stroke. Additional data from the VACS study (*J. Gen. Intern. Med.* 2005;20:1142-5) indicated that mortality in HIV patients was more than twice as high among current smokers as in pa-

tients who had never smoked (5.4 vs. 2.5 deaths per 100 person-years).

One way to apply primary care guidelines to HIV patients is to consider the "payoff time," Dr. Justice said. The payoff time is the estimated number of years of a patient's life during which the benefits of treating a comorbid condition outweigh the short-term harms.

Thus the value of screening procedures such as colonoscopy depends on the life expectancy related to a comorbid disease as well as HIV. For example, if a 50-year-old HIV-positive man is likely to die from HIV before treatment for colon cancer, if found, would reduce his risk of death from colon cancer, it may not be worth putting him through the discomfort and risk of a colonoscopy, Dr. Justice suggested. ■

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Positive Affect May Influence the Rate of HIV Progression

BY TIMOTHY F. KIRN
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SAN FRANCISCO — Depression and stress appear to be important considerations in the treatment of HIV-infected patients, Dr. Frederick Hecht said at a meeting on HIV management sponsored by the University of California, San Francisco.

Although research on the topic is not conclusive, available evidence suggests that a patient's ability to experience positive emotions may be somewhat protective against CD4 cell count loss, he said.

And, in a small pilot study of yoga practice, he obtained intriguing, but not definitive, evidence that there might be ways to mitigate depression and response to stress without writing a prescription.

The first studies that found an association between depression and CD4 cell loss were published in 1993, but they were not entirely convincing, said Dr. Hecht, research director of the UCSF Osher Center for Integrative Medicine.

Subsequent studies have suggested that it is not depression per se that is associated with rapid HIV disease progression, and that negative affective symptoms have little or no impact on HIV progression.

Instead, these studies have shown that positive affect—in other words, the ability to experience positive thoughts and emotions, and to enjoy some aspects of life despite also feeling sadness—can have a large effect, Dr. Hecht said.

One study, the San Francisco Men's Health Study, included 407 HIV-positive men who were followed over a period of 10 years. The relative risk of AIDS mortality was 0.89 in those who had high scores on positive affect measures. Negative affect, however, had little relationship to mortality (*Psychosom. Med.* 2003;65:620-66).

In another study, of 82 HIV-positive men followed for an average of 5 years, the presence of stress was associated with risk of progression. One major stressful

event in a 6-month period, such as the dissolution of an intimate relationship or loss of a loved one, doubled the risk of disease progression.

Studies done by researchers at the University of California, Los Angeles, have hinted at how

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mood and affect might be tied to the immune system in the setting of HIV infection. That research has suggested that the connection might be through the CCR5 receptor, the major coreceptor of HIV on CD4 cells. Persons who have rapidly progressing disease may have more CCR5 receptors, and the researchers have shown that neurotransmitters such as norepinephrine can increase receptor expression in vitro.

In an intriguing study, those researchers found that a high lev-

el of autonomic nervous system activity, as would be seen in times of stress, impairs response to highly active antiretroviral therapy and increases virus levels (*Proc. Natl. Acad. Sci. U.S.A.* 2001; 98:12695-700).

In his unpublished study of yoga practice, Dr. Hecht assigned 23 HIV-infected patients to a group that practiced yoga three times a week, and 25 others to a control group.

At the end of 3 months, both groups had improvement in their positive and negative affect scores on a test known as the Positive and Negative Affect Schedule, but the mean improvement for the group that practiced yoga was eight times greater on positive affect and twice as great on negative affect.

The yoga group had an increase in average CD4 cell level, while the control group had a decrease, but the difference was not statistically significant, Dr. Hecht said.

"There's at least a little bit of

preliminary evidence that interventions like this yoga intervention might have some effect on CD4 cell counts," he said.

Dr. Hecht said that he uses this information when treating his own HIV patients. He advises them that withdrawing from life in order to avoid stressors is not advisable, but that chronic stress or depression do need to be addressed.

He does not mislead them into thinking that by developing positive affect they can prevent progression. "The issue here is really rate of progression, not whether you progress or not," he said.

Antidepressant treatment probably does not have a benefit, Dr. Hecht added. In a study of HIV patients put on a selective serotonin reuptake inhibitor, there was no significant effect on T-cell levels (*J. Clin. Psychiatry* 1994;55:92-7).

That study may not have been large enough to detect an improvement. But it may also indicate that antidepressants have no appreciable impact on positive affect, he said. ■