



Emerging Issues in Research, Treatment, and Care

**Manali
Nekkanti, MPH**

Thanks to better HIV treatments—and the efforts of treatment advocates—people are living longer with HIV. As HIV positive people get older, and as increasing numbers of people acquire HIV at an older age, the medical, emotional, and social issues typically associated with aging are compounded by HIV-related challenges.

To address these issues, San Francisco AIDS Foundation held an official satellite session at the XVIII International AIDS Conference on July 19, 2010, in Vienna, Austria. The session included a series of presentations on current epidemiology and research, followed by a panel discussion with older HIV positive individuals and a dialogue with audience members.

The satellite session was cosponsored by Gay Men's Health Crisis and amfAR, the Foundation for AIDS Research. Dr. Rowena Johnston, Vice President and Director of Research at amfAR, gave the audience an epidemiological overview of HIV/AIDS in older individuals around the world. She was followed by Dr. Amy Justice, Associate Professor of Internal Medicine at Yale Medical School and Principal Investigator for the Veterans Aging Cohort Study, who offered a framework for understanding the multiple illnesses that affect people aging with HIV. Dr. Glenn Treisman, Director of the AIDS Psychiatry Program at Johns Hopkins University School of Medicine, spoke on the interactions between HIV disease and psychiatric conditions.

These presentations were followed by a discussion among HIV/AIDS advocates who are themselves over the age of 50 and living with HIV. Dr. Michael Siever, Director of Behavioral Health Services at San Francisco AIDS Foundation, and Ms. Sylvia Young, Peer Advocate Program Manager at Women Organized to Respond to Life-threatening Disease (WORLD) in Oakland, California, were joined by Ms. Siphwe Hlophe, Founder and Director of Swaziland Positive Living (SWAPOL).

Following are excerpts from the presentations and the panel and audience discussions, highlighting important issues and urgent questions around aging and HIV.

EPIDEMIOLOGY OF HIV AND AGING

“As antiretroviral therapy becomes more widely available, the proportion of people with HIV who are over 50 will absolutely grow.”

—Rowena Johnston

In her overview presentation, Dr. Rowena Johnston cited a report from the Centers for Disease Control and Prevention (CDC) indicating that, in the United States, 28% of new HIV diagnoses in 2006 were among people over 45 years of age. Mathematical models suggest that half of all HIV positive individuals in the U.S. will be over 50 by the year 2015.

Data collected by the Joint United Nations Programme on AIDS (UNAIDS) define “adults” as people between 15 and 49 years of age, making it difficult to find information about HIV infection in people over 50 outside the U.S. But a study described in the journal *Clinical Interventions*

in Aging suggests that about 7% of the world's HIV positive population (roughly 2.3 million people) is 50 or older. That proportion will increase as antiretroviral therapy becomes more widely available around the globe and more people have access to life-saving treatment. Already, Johnston said, there are significant populations of older adults living with HIV in Kenya, Jamaica, India, and parts of East Asia.

Where data about HIV in older adults *are* available, they tend to reflect prevalence (the number of people living with HIV disease) rather than incidence (the number of people newly infected), making it unclear whether HIV was acquired earlier in life or after the age of 50. This gap in knowledge poses a problem, as the medical needs of individuals newly infected with HIV

in older age tend to differ from those of older adults who have lived with the virus for many years.

There is also a great need for HIV prevention efforts among older populations. HIV prevention messages rarely target older individuals because of a common assumption that they don't have sex—a misconception flouted by a recent study published in the *New England Journal of Medicine* showing that 73% of people aged 57 to 64 years are sexually active. "I think that probably comes as a surprise to a lot of people," said Johnston. Yet older adults often do not consider themselves at risk for HIV or other sexually transmitted infections; Johnston cited an Australian study suggesting that few older people use condoms or seek HIV testing.

As antiretroviral therapy becomes more widely available and people live longer with HIV, Johnston concluded, more information on the epidemiology of HIV and aging will be necessary to adequately meet the HIV treatment and prevention needs of older adults around the world.

COMORBIDITIES ASSOCIATED WITH HIV AND AGING

"The question really is, 'What's the total burden of disease, and how do we try to minimize its effects on people's quality of life and survival?'"

—Amy Justice

Between 20% and 75% of deaths among HIV positive individuals on antiretroviral treatment are now due to causes other than the AIDS-defining conditions specified by the CDC, explained Dr. Amy Justice, citing data from several studies showing that major causes of death among people with HIV are attributable to alcohol use, liver disease, cardiovascular disease, cancer, and renal disease. She stressed, however, that while these illnesses are not considered AIDS-defining conditions, they are not necessarily unrelated to HIV disease.

Differences in HIV-related mortality between younger and older age groups cannot be explained by age alone. "Clearly, folks who have HIV infection—and people who have lived an extended period of time exposed to HIV infection—are *biologically* older than people who are newly infected or are not infected," Justice explained, and life expectancy may be shorter even among optimally treated individuals.

Researchers once thought that antiretroviral drug toxicities accounted for the continued higher risk of illness and death among treated patients. But results from the Strategies for Management of Antiretroviral Therapy (SMART) study, first published in 2006, suggested otherwise.

INFLAMMATION AND IMMUNE ACTIVATION

When the body is infected with bacteria or viruses (such as HIV), cells in the immune system produce proteins called *cytokines*. These proteins act like chemical "messengers" and help organize the body's immune response. Some cytokines trigger *inflammation*, which involves the transport of cells and fluids to the site of the injury; this causes the warmth, redness, swelling, and soreness you may notice around a cut as it heals.

Inflammation can occur not only at the level of your skin or in response to a visible injury, but also in organs or body systems such as the immune system or the central nervous system—and may last far longer than the time it takes for a cut to heal. Chronic inflammation, which is now known to be associated with HIV infection, persists over time and involves the continued healing and destruction of cells and tissues. This type of inflammation is thought to be linked to heart disease and other life-threatening conditions.

Like inflammation, *immune activation* is appearing more and more frequently in the HIV literature. Soon after HIV infection occurs, massive numbers of immune cells in the gut are destroyed, allowing bacteria that normally live in the intestines to leak into the bloodstream—a process called "microbial translocation." HIV is also thought to interfere with certain cells, called "regulatory T-cells," which are essential to halting immune responses once an infection is eliminated from the body. Both microbial translocation and the dysfunction of regulatory T-cells appear to contribute to immune activation, and to an overstimulated and overworked immune system.

In this landmark study, individuals who interrupted antiretroviral treatment when their CD4 counts exceeded a set threshold *still* had more deaths and more AIDS-defining and non-AIDS-defining conditions than study participants who stayed on continuous treatment, suggesting that long-term exposure to the virus itself accounts—at least in part—for the higher rates of illness and death seen among HIV positive individuals.

Today, researchers believe that HIV increases the risk of many “non-AIDS conditions,” and chronic inflammation and immune activation appear to play a significant role (see sidebar, page 43). The relative risk contributed by HIV infection is modest compared with other established risk factors for these conditions, but the effect of HIV increases over time: the longer an individual has the virus, the greater his or her risk for such conditions compared with a non-infected person.

The list of comorbidities (diseases or conditions that coexist with a primary disease) associated with HIV includes diseases of the lungs, liver, kidneys, and heart and blood vessels, as well as neurological conditions and bone diseases. Clinicians with HIV positive clients need to carefully monitor for early signs of these non-AIDS conditions, Justice said, because they can be used to predict HIV disease progression and help providers intervene and work with patients to improve life expectancy and quality of life. For example, some conditions may justify starting antiretroviral therapy early, and conditions such as anemia may become important indicators of HIV disease progression.

Justice also acknowledged that drug toxicities complicate treatment for HIV positive individuals with comorbid conditions, and stressed that individualized care is becoming increasingly important. “If someone

already has renal injury, we probably want to avoid drugs that are going to add to that renal injury, but all else equal, those drugs may actually help *reverse* some of that injury,” she explained. “It’s getting more complicated, in the sense of the balance that we need to make and the tailoring that we need to do for each individual patient who comes in.”

MENTAL HEALTH AND HIV

“If you treat psychiatric disorders, [HIV] patients do better.”

—Glenn Treisman

Drawing on his work at Johns Hopkins, Dr. Glenn Treisman focused on three key mental health issues that influence HIV disease: depression, cognitive impairment, and substance use, all of which may increase with age and affect treatment adherence, viral load and CD4 cell counts, inflammation in the central nervous system (CNS), and CNS infection.

Depression, Treisman said, is common in the setting of HIV infection—occurring six to ten times as frequently in aging HIV-infected patients compared with the general population, he estimated. Unfortunately, he explained, depressed patients tend to be less adherent to antiretroviral therapy and other medical treatments and less likely to seek care. Depression can also worsen cognitive function (and be worsened by cognitive decline) and intensifies substance use disorders.

There is also good reason to believe that the virus itself can cause depression, Treisman said, citing studies that link HIV-induced cytokine activity and CNS inflammation to depression in a large subset of patients. HIV and depression thus appear to perpetuate one another: as Treisman put it, the virus “inflames your brain [and] causes depression. As you get depressed, you don’t take your HIV medicines, and

as you don’t take your HIV medicines, your depression gets worse.”

Another issue often faced by people aging with HIV is cognitive impairment. “Even though we’re treating people, we still see them getting cognitively impaired—it’s just more subtle forms of cognitive impairment... and the onset is more variable,” said Treisman. People with cognitive impairment may experience a general slowing of their thought processes, along with poor coordination, memory loss, and depression.

According to a recent study described in *American Journal of Geriatric Psychiatry*, cognitive impairment also has a greater effect on treatment adherence in older people, putting them at higher risk for drug resistance and poorer suppression of HIV.

HIV-associated dementia, an advanced form of cognitive impairment, is associated with elevated viral load in the central nervous system. New research is examining whether antiretroviral regimens that better penetrate the CNS may decrease the risk for HIV dementia—as well as depression. Treisman cited unpublished data from Scott Letendre at the University of California, San Diego, whose research suggests that better CNS penetration of antiretroviral drugs is correlated with improved mood. With drugs that can reach HIV in the CNS and halt its replication there, Treisman said, “not only do we prevent dementia, but we may be preventing depression—which isn’t a surprise to those of us who subscribe to the ‘cytokine idea’ that depression is caused by elevated cytokines in your brain.”

Substance use and addiction represent another mental health issue that disproportionately affects people aging with HIV, Treisman observed, although there is a lack of recognition among health providers that substance abuse is an issue for older patients. Chronic use of opiates such as oxycodone (OxyContin and other formulations)

may not be considered “addiction,” but it does affect cognition and has a negative effect on HIV health, Treisman noted. Substance-use treatment is a cost-effective but chronically underfunded intervention.

“We *can* get people better—all of the things I talked about tonight are treatable,” concluded Treisman. “Demand more resources for your patients, and raise a little hell when people say, ‘They’re old anyway.’”

CHALLENGES AND RESILIENCIES

“I never thought I would have to worry about this: Who is going to take care of me as I get older?”

—Michael Siever

Following the presentations, the three panel participants gave personal accounts of some of the challenges they are experiencing as they get older with HIV. Dr. Michael Siever prefaced his comments by acknowledging that, being a white male from a wealthy country and having been fortunate enough to receive and respond well to antiretroviral treatment, he speaks from a position of privilege and is extremely grateful to have lived long enough to face these challenges. Then he summed up some of the confusion felt by HIV positive people experiencing health problems as they get older: “Is it age or AIDS?”

Researchers are grappling with the same question about the interactions of HIV, HIV drugs, and aging, but it is unclear just what the study findings mean to older HIV positive people. Siever spoke of the difficulty interpreting the flood of new research reports on HIV and aging, particularly around HIV-induced inflammation. As he put it, “sometimes too much knowledge is not very helpful.”

Sylvia Young admitted that the challenges she encounters as an older HIV positive person sometimes seem

endless. She related that a diagnosis of oral cancer the previous year led to three surgeries and loss of speech for two weeks, which in turn led to depression. She battled the depression with exercise, until the exercise caused debilitating fatigue. “It’s one thing after another,” she said.

All three panelists also talked about the stigma that older HIV positive people often encounter. As a gay man getting older with HIV, Siever faces homophobia, HIV stigma, and ageism—sometimes from within the gay community itself: “There’s an incredible amount of ageism in the gay community, where we are, unfortunately, all expected to be young and beautiful and have rippling abs and all kinds of impossible things to have when you’re 60.”

In his clinical work, Siever sees increasing numbers of older gay men using alcohol and drugs as a way of coping with stigma. He finds it especially painful when older men who have recently “come out” turn to substance use to ease the transition into the gay community, or feel that they won’t appeal to potential sex partners unless they offer drugs.

In her work with SWAPOL, Siphwe Hlophe has seen HIV stigma provoke intimate partner violence. “The most important thing [is] disclosure to your partner,” she said, relating that, in her experience, some male partners—even those living with the virus themselves—blame women for testing positive.

Hlophe was one of the first women in Swaziland to publicly declare her HIV positive status, and her organization now teaches women to fight stigma in the home and in their communities, as well as in health clinics, where SWAPOL-trained “lay counselors” help HIV positive women get better care as they age. Through SWAPOL, women gain the resilience to live longer with HIV.

“We empower women on issues of HIV and AIDS,” Hlophe explained, “especially those over 60, who have started their income-generating project, so that you don’t think about the disease—you think about what you are doing now in order to earn a living.”

Young offered a similar view: “In my work at WORLD, as a peer advocate working with women who are over 50 and HIV positive, I have seen challenges, but I also see resilience.”

Working with a peer advocate, Young explained, helps older HIV positive women get better attention to their unique health needs—such as starting menopause in their early forties, or dealing with arthritis and incorporating pain medication into their daily treatment regimen for HIV. “I have seen peer advocacy change the lives of positive women,” she said.

MOVING FORWARD

“The good news is, we have to think about HIV and aging.”

—Amy Justice

So, what should advocates, providers, individuals, and communities be doing *now* to prepare for and meet the needs of an increasingly older HIV positive population?

Siever, Young, and Hlophe agreed that a major advocacy priority is overcoming the misconception that HIV does not affect older people. They also emphasized the importance of addressing the larger issues of poverty, racism, sexism, and ageism, all of which hinder efforts to prevent new HIV infections and improve the health and wellness of those already living with the virus.

Returning to the topic of mental health, Treisman noted that providers often hesitate to offer antidepressant medications to elderly patients because older persons tend to experience more side effects and are generally more resistant to taking psychiatric drugs. He

and Justice concurred that, rather than following a single “recipe” for treating all HIV patients regardless of age, providers should tailor care for each individual. Treisman also encouraged providers to look beyond a patient’s HIV to ensure that other conditions don’t go untreated.

In a similar vein, Justice suggested that providers and individuals draw on resources outside of HIV medicine—specifically, the field of geriatrics.

For example, falls prevention (such as removing throw rugs and other tripping hazards from the home) is one proactive step that older adults and their health care providers can consider.

“We should be thinking about bone mineral density and thinking about medications,” said Justice, “but we also ought to think about the living environment that this person is in: Can we help them *prevent* having a fall rather than treating it after it occurs, when they have a fracture?”

Justice and Treisman agreed that other fairly simple measures—such as promoting activities for mental stimulation and switching to clothing with easy-to-manipulate Velcro fasteners

rather than buttons—can help aging HIV positive individuals prepare for and cope with cognitive impairment. “There are lots of resources for elderly patients that are going to be necessary in somewhat younger HIV patients,” Treisman concluded.

In terms of what communities can do, one audience member recalled the early days of the HIV epidemic in the U.S., when members of the gay community assumed caretaking responsibilities for their sick and dying friends. His suggestion for meeting the needs of an aging HIV positive population was simple but poignant: “It’s time to take care of each other again.”

Manali Nekkanti, MPH, is a research associate at San Francisco AIDS Foundation.

Selected Sources

Bourne, C. and V. Minichiello. Sexual behavior and diagnosis of people over the age of 50 attending a sexual health clinic. *Australian Journal on Ageing* 28(1):32–36. March 2009.

Centers for Disease Control and Prevention. Estimates of new HIV infections in the United States. August 2008. www.cdc.gov/hiv/topics/surveillance/resources/factsheets/pdf/incidence.pdf.

Ettenhofer, M. and others. Aging, neurocognition, and medication adherence in HIV infection. *American Journal of Geriatric Psychiatry* 17(4):281–90. April 2009.

Kautz, T. and others. AIDS and declining support for dependent elderly people in Africa: retrospective analysis using demographic and health surveys. *British Medical Journal* 340:c2841. June 16, 2010.

Kirk, J. and M. Goetz. Human immunodeficiency virus in an aging population, a complication of success. *Journal of the American Geriatric Society* 57(11):2129–39. November 2009.

Letendre, S. and others. Validation of the CNS Penetration-Effectiveness rank for quantifying antiretroviral penetration into the central nervous system. *Annals of Neurology* 65(1):65–70. January 2008.

Letendre, S. and others. Enhancing antiretroviral therapy for human immunodeficiency virus cognitive disorders. *Annals of Neurology* 56(3):416–23. September 2004.

Lindau, S. and P. Schumm. A study of sexuality and health among older adults in the United States. *New England Journal of Medicine* 357(8):762–74. August 23, 2007.

Martínez, E. and others. Incidence and causes of death in HIV-infected persons receiving highly active antiretroviral therapy compared with estimates for the general population of similar age and from the same geographical area. *HIV Medicine* 8(4):251–58. May 2007.

Nguyen, N. and M. Holodny. HIV infection in the elderly. *Clinical Interventions in Aging* 3(3):453–472. October 2008.

O’Brien, S. and others. Cytokines: abnormalities in major depression and implications for pharmacological treatment. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 31(5):1044–53. June 30, 2007.

Palella, F. Jr. and others. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV Outpatient Study. *Journal of Acquired Immune Deficiency Syndromes* 43(1):27–34. September 2006.

Sackoff, J. and others. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. *Annals of Internal Medicine* 145(6):397–406. September 2006.

Smit, C. and others. Effective therapy has altered the spectrum of cause-specific mortality following HIV seroconversion. *AIDS* 20(5):741–49. March 21, 2006.

Strategies for Management of Antiretroviral Therapy (SMART) Study Group. CD4+ count-guided interruption of antiretroviral treatment. *New England Journal of Medicine* 355(22):2283–96. November 30, 2006.

FOR MORE INFORMATION ON AGING AND HIV

On October 13, 2010, San Francisco AIDS Foundation and several community partners held a public forum, titled “HIV & Aging: Now What?”

The forum brought together community members, advocates, health care and service providers, and researchers for a dialog about the challenges of getting older with HIV and the latest research on HIV and aging.

This event was part of the foundation’s HIVision forum series, which provides a safe venue for discussion of timely and potentially controversial topics in HIV prevention, treatment, and care.

To download the executive summary of the forum and learn more about past and upcoming HIVision events, visit www.sfaf.org/HIVision.