# Immune Systems of HIV Patients Age Rapidly

BY SHERRY BOSCHERT

SAN FRANCISCO — Antiretroviral therapy has allowed many HIV-infected people to live long enough to grow old, yet their immune systems seem to age rapidly for their chronologic age, a factor that appears to be contributing to increased risks for non-HIV diseases of aging in middle-aged patients, according to several speakers at a meeting on the medical management of HIV and AIDS sponsored by the University of California, San Francisco.

"There are striking similarities between the immune systems of some of our patients in their 50s and [those of] their parents," said Dr. Steven G. Deeks, professor of medicine at the university.

In 2007, 28% of people living with HIV were aged 50 years or older; that proportion will grow to 50% by 2015, Dr. Richard Brooks, also of the university, said in a separate presentation.

Also at the meeting, Dr. Toby Maurer reported that her clinic is seeing more HIV-infected patients with skin diseases associated with aging, including disseminated herpes zoster and indolent Kaposi's sarcoma, despite relatively healthy CD4 counts ranging between 300 and 700 cells/mm$^3$ and viral suppression on at least 18 months of antiretroviral therapy.

Disseminated zoster is "very unusual with a CD4 count of 350 cells/mm$^3$" or more, said Dr. Maurer, director of dermatology at San Francisco General Hospital. "Is [this finding] another indication of abnormal immune aging? I don't know, but it's something to think about."

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The Kaposi's sarcoma cases are not the aggressive variety seen 20 years ago in HIV-infected patients, she said, but are the type typically found in older Mediterranean men.

To preserve immune function, Dr. Deeks advocates starting highly active antiretroviral therapy (HAART) in any HIV-infected patient who is motivated to begin treatment—a more aggressive approach than called for in treatment guidelines.

HAART reduces but does not eliminate T-cell activation and inflammation. Persistent, residual inflammation while on HAART is more extensive when patients start therapy at CD4 counts less than 200 copies/mm$^3$. "The longer you wait to start therapy, the more immunologic harm that's done," he said. The consequences of the inflammatory process are even worse for people with comorbid conditions such as heart disease or cancer.

Previous attempts to reduce HIV-associated immunosenescence and inflammation through the use of prednisone, hydroxyurea, cyclosporin, or mycophenolic acid were "like treating a subtle problem with sledgehammers," Dr. Deeks said.

"We need to reduce inflammation in a safe way" through the use of statins, aspirin, exercise, omega-3 fatty acids, vitamins, and immunomodulators, he said. Newer strategies could include investigational drugs that enhance recovery of CD4 cells or that fully eradicate the subtle levels of persistent or replicating virus.

An "overwhelming amount of data" show that even patients with undetectable virus and increased CD4 counts on HAART are more likely than people without HIV to develop heart disease, non-AIDS cancer, bone disease and fractures, left ventricular dysfunction, liver or kidney failure, and frailty, Dr. Deeks said.

After controlling for the effects of other factors, including lipids or hypertension, HIV-infected patients have a 75% higher risk for cardiovascular events than do uninfected people, several studies suggest.

Dr. Brooks noted that frailty was 11 times more common in HIV-positive men, compared with HIV-negative men, in one study (J. Gerontol. A Biol. Sci. Med. Sci. 2007;62:1279-86). HIV infection of 4 years' duration or less conferred a risk for frailty in a 55-year-old man that compared with risks for a 65-year-old HIV-negative man, "confirming our impression that HIV-positive men are aging faster than their HIV-negative counterparts," said Dr. Brooks.

To help HIV-infected patients stay healthy longer, he advised focusing on modification of traditional risk factors for non-HIV comorbidities of aging—smoking, hypertension, dyslipidemia, weight gain, diet, and exercise.

When possible, avoid HIV medications that can exacerbate illnesses associated with aging and check for drug-drug interactions, he added. Older protease inhibitors and zidovudine increase the risk for insulin resistance. Abacavir, didanosine, and protease inhibitors increase risk for cardiovascular disease. Zidovudine, protease inhibitors, and nonnucleoside reverse transcriptase inhibitors increase risk for dyslipidemia.

Dr. Deeks has been an adviser to GlaxoSmithKline and received research funds from Pfizer, Merck, Gilead, and Bristol-Myers Squibb. Dr. Maurer and Dr. Brooks reported having no conflicts of interest. ■

# Condoms Provide Partial Protection Against HSV-2

BY BRUCE JANCIN

BERLIN — Consistent use of condoms has a moderate protective effect against acquisition of herpes simplex virus 2, the leading cause of genital ulcer disease worldwide.

A recent pooled analysis of six prospective studies concluded that men and women who used condoms 100% of the time during sex had a 30% lower risk of HSV-2 acquisition than people who never used condoms, Dr. Laurence Le Cleach said at the annual congress of the European Academy of Dermatology and Venereology.

The pooled analysis by investigators at the University of Washington, Seattle, showed that the relationship between condom usage and HSV-2 acquisition was roughly linear. Thus, individuals who used condoms one-quarter of the time they engaged in vaginal or anal intercourse had a 7% lower relative risk of HSV-2 acquisition than never users, while those who used condoms half the time had roughly a 15% risk reduction, noted Dr. Le Cleach of Central Hospital South in Corbeil-Essonnes, France.

The analysis included three HSV-2 candidate vaccine trials, an antiviral drug study, a behavioral intervention trial, and an observational study. Collectively, the studies involved 5,384 participants who were HSV-2–negative at baseline. During more than 2 million days of follow-up, 415 laboratory-confirmed cases of HSV-2 infection occurred (Arch. Intern. Med. 2009;169:1233-40).

The impetus for the analysis was a report by a National Institute of Allergy and Infectious Diseases panel that there was insufficient evidence to conclude condoms prevent HSV-2 acquisition. The pooled analysis provides solid data demonstrating that there is, in fact, a benefit. Physician recommendations to both men and women in serodiscordant relationships that they consistently use condoms to reduce their risk of HSV-2 acquisition would have a substantial public health benefit, she said.

The 30% reduction in risk of HSV-2 acquisition with consistent use of condoms is a considerably less robust protective effect than shown in other studies involving the use of condoms to protect against other sexually transmitted infections. The explanation is thought to be that HIV is transmitted through contact with bodily fluids, while HSV-2 can be transmitted through skin-to-skin or skin-to-mucosa contact involving surfaces not covered by the condom. ■

# *Study Evaluates Commuting Patterns and Pandemic Spread*

BY DOUG BRUNK

A method of modeling global pandemic patterns has found that local commuting patterns provide a strong correlation and synchrony in the evolution of an emerging disease at the local level and during the tail end of disease spread.

The finding runs counter to previous studies that have suggested that long-range airline traffic marks the primary predictor of global disease spread, researchers led by Alessandro Vespignani, Ph.D., reported (PNAS 2009 Dec. 14 [doi:10.1073/pnas.0906910106]).

"On the one hand, the global epidemic behavior is governed by the long-range airline traffic that determines the arrival of infectious individuals on a worldwide scale," the researchers stated. "At the local level, however, the short-range epidemic coupling induced by commuting flows creates a synchrony between neighboring regions and a local diffusive pattern with the epidemic flowing from subpopulations with major hubs into the neighboring subpopulations."

Dr. Vespignani of the Indiana University School of Informatics and Computing, Bloomington, and his associates collected short-range commuting data (defined as a distance of up to 300 km) from 29 countries on five continents.

They used the information to create a mathematical model of the commuting behavior of specific populations of people in 220 countries living near 3,362 airports. The model included a seasonal dependence of disease transmission.

The researchers found that while commuting flows were, on average, one order of magnitude larger than the long-range airline traffic, "the global spatiotemporal patterns of disease-spreading are mainly determined by the airline network. Short-range commuting interactions have, on the other hand, a role in defining a larger degree of synchronization of nearby subpopulations and specific regions, which can be considered weakly connected by the airline" network.

Dr. Vespignani and his colleagues concluded that their model offers "an initial understanding of the level of data integration required to obtain reliable results in large-scale modeling of infectious diseases."

The study was supported by funds from the National Institutes of Health and the Lilly Endowment Grant. In addition, Dr. Vespignani was supported by a Defense Threat Reduction Agency Grant and by a Future Emerging Technologies contract from Epiwork, while a coauthor was supported by a contract from the European Research Council. ■