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Protease inhibitors: Emerging research explores possible link with heart disease

Experts say PI therapy remains essential for most

Researchers have given clinicians a mixed view of HIV disease and coronary heart disease risk, including evidence that protease inhibitors increase the risk of heart disease. The problem isn't the evidence, but perspective, two investigators say.

"Antiretroviral therapy, be it protease inhibitors or nucleoside reverse transcriptase inhibitors, is highly effective at reducing morbidity and mortality from AIDS," says **Carl Grunfeld**, MD, PhD, a professor of medicine and division chief at the Veterans Affairs Medical Center (VAMC) in San Francisco, CA.

"This is huge compared to the small increase from cardiovascular risk," Grunfeld says. "Nonetheless, there is a small increase in cardiovascular risk in every study, although studies disagree on how much affect protease inhibitors have."

One recent study examines the 10-year predicted coronary heart disease risk of HIV-infected men and women and finds PI use does increase risk.¹

"I think the totality of the best evidence we have now suggests there may be some harmful effects of PIs, as our data suggested, but there's more evidence suggesting the opposite," says **Robert Kaplan**, PhD, an associate professor of epidemiology at Albert Einstein College of Medicine in the Bronx, NY. Kaplan has co-authored a number of studies on this topic, including the recent 10-year predictive study.

Some studies show that ART can reduce cardiovascular disease substantially, Kaplan notes.

"We really try to emphasize that ART exposure is a small and uncertain piece of the picture here," Kaplan says.

Grunfeld, who treats cardiovascular patients including many infected with HIV, focused his research on the association between HIV infection, PI use, and fibrinogen levels. His recent study found that PI use is associated with elevated fibrinogen levels, and these might contribute to increased risk of atherosclerosis in patients who are HIV infected.²

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"This is the first study with a possible explanation for how PIs cause an increase in atherosclerosis risk," Grunfeld says.

Fibrinogen is a clotting agent that is a useful tool in the body until there's a plaque that ruptures, Grunfeld explains.

"If you have a clot and it ruptures and you have high levels of fibrinogen then you're more likely to form a clot and have a heart attack," he says.

The fibrinogen levels are not as important for

healthy individuals who do not have arteriosclerosis, but these can be a factor for those who already have lifestyle and other factors placing them at risk for heart disease, Grunfeld adds.

"I think people are increasingly aware that there's an increased risk of heart attacks and coronary problems with HIV infection," he says. "So they should aggressively look at reducing risk factors of arteriosclerosis by controlling blood pressure, cholesterol, and stop smoking."

There are many well-established factors that predict heart disease, including smoking and obesity, Kaplan notes.

A factor like fibrinogen is not well understood, and there are no medications to treat for fibrinogen problems, he says.

Also, while there is evidence that high fibrinogen levels are linked to heart disease in non-HIV patients, there is no evidence that high levels of fibrinogen in HIV patients is linked to heart disease, Kaplan adds.

In research that will be published later this year, Kaplan and co-investigators have found that classic vascular risk factors, such as being overweight, smoking, high blood pressure, and high cholesterol, were much more consistent with heart disease risk than HIV medications.

"The patients with the worst HIV disease had the highest rate of vascular disease or arteriosclerosis in that research," Kaplan says.

However, what both recently-published studies suggest is that HIV clinicians need to pay particular attention to cardiovascular risk factors, including any impact on the risk by HIV drugs — whether these are positive or negative.

The key point is that there's an increased risk of heart attacks and coronary problems with HIV infection, and clinicians should aggressively look at reducing risk factors of arteriosclerosis, Grunfeld says.

"They need to control blood pressure and cholesterol and have patients quit smoking," he says. "Most studies where HIV patients are compared to controls show they smoke twice as much as controls, and we don't know why."

Grunfeld aggressively works to prevent cardiovascular disease in his endocrinology clinic, where one-third of patients have HIV infection.

"I try to teach my residents and fellows to be aggressive about preventing heart disease, and I practice what I preach," Grunfeld says. "I eat a healthy diet so I can say to patients 'This is what I do; I don't smoke, and I run and exercise, leading by example.'"

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Editorial Questions?

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HIV patients who smoke are offered every intervention available, including counseling with behavioral modification professionals and a nicotine patch.

Grunfeld hasn't studied patient outcomes from his educational efforts, but he has had patients who've quit smoking.

Grunfeld also encourages patients to start walking and aim for a daily walk so that if they miss one or two, they'll still be exercising at least five times a week, as is recommended by national public health guidelines. And HIV patients are prescribed the statin drugs that are suitable for patients who are also on ARTs.

However, there is one risk factor for which there is no intervention: "Age is the strongest risk factor," Grunfeld says. "As you get older the mainstay is to treat cholesterol, treat blood pressure, and stop smoking."

HIV clinicians who are treating older patients might have to consider the impact of PIs and other ARTs on heart disease risk when all other efforts to reduce risk have been exhausted.

"If someone has a CD4 cell count of 10 and is on salvage therapy, then it's much more important to get the best HIV treatment," Grunfeld says. "But many of our patients will live and not be harmed by the consequences of HIV for a long time, and I don't want them harmed by heart disease."

Grunfeld uses the Framingham equation to predict patients' heart disease risk and to guide his decisions about how aggressively to treat them for heart disease prevention.³

"One thing of interest for clinicians is as their treated populations age and other vascular diseases come on the rise, then there might be more rationale for worrying about potential risks associated with certain medicines," Kaplan says. "But for the larger number of patients who are middle-aged or young, the dangers associated with inadequate control of their HIV disease far outweigh any hypothetical risks of heart disease."

References

1. Kaplan RC, Kingsley LA, Sharrett AR, et al. Ten-year predicted coronary heart disease risk in HIV-infected men and women. *Clin Infect Dis*. 2007;45(8):1074-1081.
2. Madden E, Grace L, Kotler DP, et al. Association of antiretroviral therapy with fibrinogen levels in HIV-infection. *AIDS*. 2008;22:707-715.
3. Dawber TR, Kannel WB, Revotskie N, et al. Some factors associated with the development of coronary heart disease. Six years' follow-up experience in the Framingham Study. *Am J Public Health* 1959;49(10):1349-1356. ■

ADHERENCE STRATEGIES

Stressful life events have profound impact on ART

Study outlines public health problem

It's no surprise to clinicians that many or most of their HIV patients are negatively impacted by major life stresses. But new research shows that HIV medication adherence among people with the most stressful lives is abysmally low.

Investigators found that 87% of HIV-infected people with six or more stressful life events were not adherent to their antiretroviral therapy (ART) within the previous two weeks, says **Jane Leserman**, PhD, a professor at the University of North Carolina at Chapel Hill.¹

"When we look at people who have either zero or one of the stressful life events we measured, about 22% of those people were not adherent in the past two weeks," Leserman says.

"So you see a huge difference," Leserman says. "My interpretation is that people who have a lot of stressful life events tend to have much more traumatic lives with all kinds of chaotic events that go on in their lives, and this interrupts their ability to be adherent to their medication."

When HIV patients are worried about where they'll sleep, or when they have huge fights with their families, then these are the pressing concerns of their day — not taking their HIV drugs, she adds.

Since HIV clinicians need their patients to achieve a 95% adherence rate to prevent the development of drug resistant strains, which can be transmitted to others, then this reaction to stressful life events is a very serious problem, Leserman says.

"We have medications to help this population, but the problem is getting people to take those meds in a regular way," Leserman adds.

The study of 105 HIV-infected men and women found that 44.8% had missed a medication dose in the previous two weeks, and 22.1% had missed a dose the previous weekend.

Adherence was measured from a questionnaire that included questions about when was the last time they missed any medications.

"If you have to have 95% adherence to prevent

the development of drug resistance, and in a two-week period almost 45% of people said they missed one of their doses — that’s bad,” Leserman says. “This tells us we need to develop interventions for adherence that really address these issues of stress.”

Researchers measured stressful life events through a modified version of the Life Events Survey. It looked at only moderate to severely stressful events based on previous research, and these included change in relationships, death or serious illness among family or close friends, work/financial problems, accidents or safety issues, crime or legal problems, and other life changes.¹

Leserman has long studied the effects of stressful events and trauma on disease progression in HIV. In a study published last fall, she showed that women and men in the rural Southeast had more traumatic life events with a faster progression in terms of all causes of AIDS.²

“We found stress was an important predictor of progression to AIDS over a nine-year period,” Leserman notes.

“The other areas where I’ve shown stress to have an impact include functioning,” she adds. “We found that stressful life events and trauma were very highly related to core functioning, such as the degree to which stress impacts your ability to carry out your daily chores, to function physically and emotionally.”

Future research will focus on the impact of stress on HIV fatigue, Leserman says.

“This population has a lot of stressful and traumatic events in their lives,” Leserman says. “In terms of depression, 21% met the criteria for depression in this study.”

The study also found that 41% had chronic financial stress, 24% had a serious argument or separation from their partner, 24% had estrangement from their family, and 19% had a major illness that was not related to HIV infection.¹

“So you get the idea that these are fairly serious kinds of stresses the subjects in our study have experienced,” Leserman says.

The HIV-infected people who participated in the study also exhibited poor health habits, including 51% who smoked cigarettes, 34.3% who used illicit drugs in the past month, and 37.6% who drank alcoholic beverages in the past month.¹

For clinicians, it’s important to monitor their HIV patients’ mental health as consistently as they monitor CD4 cell counts, Leserman says.

“It’s important to ask about stressful events,

depression, post-traumatic stress disorder,” she explains. “Obviously, physicians can’t treat everything and may not be trained to treat the mental health, but they can refer patients to other types of services that would provide interventions in adherence.”

Adherence counseling and psychological services should be an integral part of HIV care because of the high percentage of HIV patients who have mental health issues, past traumas, and stressful life events, Leserman says.

Investigators are exploring an intervention in which HIV patients write about their trauma and stress in their lives and write about their daily life events to see if the act of writing about these will have a positive affect, she adds.

“We need to address mental health issues and stressful life events, as well as patients’ CD4 cell count and viral load,” Leserman says.

References

1. Leserman J, Ironson G, O’Cleirigh C, et al. Stressful life events and adherence in HIV. *AIDS Patient Care STDS*. 2008;22(5):1-9.

2. Pence BW, Reif S, Whetten K, et al. Minorities, the poor, and survivors of abuse: HIV-infected patients in the US deep South. *South Med J*. 2007;100(11):1114-1122. ■

Congress questions effect of abstinence-only approach

Scientists, others say programs fail to work

On the heels of Centers for Disease Control and Prevention (CDC) data showing that one in four teenage girls has a sexually transmitted disease (STD) and that nearly a third of American girls becomes pregnant as a teenager, scientists and other experts testified about abstinence-only programs at a Congressional hearing.

“For African-American and Latina girls, the [pregnancy] rate is 50%,” U.S. Rep. **Henry A. Waxman** said in an opening statement at the hearing on April 23, 2008. Waxman is chair of the Committee on Oversight and Government Reform, which held a hearing on the topic of “Domestic Abstinence-Only Programs: Assessing the Evidence.”

Domestic abstinence-only programs have received more than \$1.3 billion in tax funds, plus millions more in state funds, while there is no

dedicated source of federal funding for comprehensive classroom sex education, Waxman said.

There is no scientific evidence that abstinence-only programs prevent STDs or pregnancy, Waxman said.

“In fact, the government’s own study showed no effect for abstinence-only programs,” he said. “In 2007, the Bush Administration released the results of a longitudinal, randomized, controlled study of four federally-funded programs. The investigators found that compared to the control group, the abstinence-only programs had no impact on whether or not participants abstained from sex. They had no impact on the age when teens started having sex. They had no impact on the number of partners. And they had no impact on rates of pregnancy or sexually transmitted disease.”

Waxman also noted serious concerns about the abstinence-only programs’ contents, including a 2004 report of his that showed false and misleading medical information in the majority of the abstinence-only curricula used most frequently by federal grantees.

AIDS Action of Washington, DC, calls for a complete end to federal funding of abstinence-only education.

“Our goal, and it’s not only AIDS Action, but many of our fellow AIDS advocacy and policy organizations, is for zero funding for abstinence-only programs and shifting those funds to promote a comprehensive approach to sex education,” says Ronald Johnson, deputy executive director of AIDS Action, which submitted a letter to Waxman for the hearing. **(See AIDS Action’s letter, p. 66.)**

An abstinence-only approach is not effective in preventing HIV infection or STDs, Johnson says. “We feel that there are studies that show an abstinence-only approach is not protective, so we favor a comprehensive approach to sex education,” Johnson says.

Such an approach would validate the delay of sexual activity, but not focus on abstinence only, he adds.

A comprehensive approach to sex education would include education about safer sex practices and how to negotiate these efforts and how to practice safer sex, Johnson says.

“Particularly when dealing with adolescents, we feel a comprehensive program that includes delaying sexual debut has an important role,” Johnson says.

At the Congressional hearing, various experts

testified about abstinence-only education and research.

Researchers from the Cochrane Collaboration conducted systematic reviews of studies evaluating the impact of abstinence-only and comprehensive programs on biological and behavioral outcomes related to HIV prevention, testified **Harvey V. Fineberg**, MD, PhD, president of the Institute of Medicine of The National Academies.¹

“In the Cochrane review of abstinence-only programs, no program showed an effect on incidence of unprotected vaginal sex, number of sex partners, condom use, or sexual initiation compared to controls,” Fineberg said.

“One evaluation found several significant adverse program effects: abstinence-only participants in this program were more likely than usual-care controls to report sexually transmitted infections, pregnancy, and increased frequency of vaginal sex,” Fineberg testified. “Overall, the authors concluded that abstinence-only programs neither reduced nor exacerbated HIV risk among participants in the U.S.”

In another evaluation of federally-funded abstinence-only programs, completed in 2007 by Mathematica Policy Research Inc., there was a multi-year, experimentally-based impact evaluation of four federally-funded abstinence-only sex education programs. Participants were randomized to abstinence-only program or control conditions.²

“Based on follow-up data collected 4-6 years after enrollment, youth in the abstinence-only program group were no more likely to have abstained from sex compared to those enrolled in the control group,” Fineberg testified. “Among those who reported having had sex, the group receiving abstinence-only education reported having similar numbers of sexual partners and similar timing of onset of sexual debut to those in the control group.”²

Further committee testimony came from **Margaret J. Blythe**, MD, FAAP, FSAM, a pediatrician and professor of pediatrics at Indiana University School of Medicine of Indianapolis, IN. Blythe is the chair for the Committee on Adolescence and discussed the American Academy of Pediatrics’ position on abstinence education.

“Comprehensive sexuality education emphasizes abstinence as the best option for adolescents, but also provides age-appropriate, medically accurate discussion and information for the prevention of sexually transmitted infections and

unintended pregnancies,” Blythe testified.

Blythe further noted that abstinence-only programs are not only ineffective, but may cause harm by providing inadequate and inaccurate information that results in participants’ failure to use safer sex practices once intercourse is initiated.

CDC data show that births to teen girls, ages 15 to 19 years, increased by 3%, which is the first increase noted since a decline began 14 years ago, Blythe said.

“A longitudinal analysis of teens and virginity pledges compared ‘pledgers’ to ‘nonpledgers’ and found at a six-year follow-up that 88% of pledgers reported experiencing premarital sex and had STI rates that, statistically, were no different from those of nonpledgers,” Blythe said.³

Charles Keckler, acting deputy assistant secretary for policy and external affairs for the Administration for Children and Families of the U.S. Department of Health and Human Services

AIDS Action cites ‘grave concern’ about abstinence-only programs

The following is an April 24, 2008 letter by Ronald Johnson, deputy executive director, AIDS Action in Washington, DC submitted to Henry Waxman, chairman Committee on Oversight and Government Reform, U.S. House of Representatives.

AIDS Action serves as the national voice for AIDS service organizations, health departments, health educators, and a diverse network of community-based organizations across the country providing services for people living with or affected by HIV/AIDS. On behalf of AIDS Action’s diverse membership organizations committed to ending the HIV/AIDS epidemic in the United States, I write to express grave concern with continued federal investment in abstinence-only-until-marriage programs. AIDS Action has long called for the elimination of funding for abstinence-only-until-marriage programs, and instead supports comprehensive prevention and sexual educational programs that are scientifically sound and effective at reducing HIV and STD transmission. The health and education of our nation’s young people must become a priority for this Congress, and we commend the Committee for holding an oversight hearing on this most critical issue.

Several federally funded research studies show that abstinence-only-until-marriage education programs are ineffective at best. They do not delay the start of sexual activity or decrease the number of sexual partners. Often they contain medically inaccurate data and do not teach youth how to protect themselves from HIV infection. Most recently, a study of abstinence-only-until-marriage programs was conducted by Mathematica Policy Research Inc. on behalf of the U.S. Department of Health and Human Services. The \$1 million study found no evidence that abstinence-only programs increase rates of sexual abstinence. The study also found that students enrolled in abstinence-only-until-marriage-education programs were far less likely to know that condoms can lower the risk of sexually transmitted diseases including HIV.

It is imperative that Congress take a hard look at this scientific evidence. It is not only unethical to deny young people life saving information and education, but reprehensible for Congress to continue spending American tax dollars on ideologically-based programs that are proven to be unsuccessful. Abstinence-only-until-marriage programs have been funded by the federal government for over 25 years. These programs have received over \$1 billion dollars under the Bush administration, all without any legitimate evidentiary support in their favor.

Our government’s irresponsible and narrow focus on abstinence-only-until-marriage education has serious consequences. HIV remains a public health crisis in America, now infecting more than 40,000 people annually. Every 13 minutes, a person in the United States is newly infected with HIV. More than one in 10 of them is under the age of 25. Not only are HIV rates on the rise, America’s youth are also facing higher rates of other sexually transmitted diseases and teen pregnancy. As STD rates rise among our nation’s youth so does their risk of HIV, as having a sexually transmitted disease makes an individual biologically more susceptible to HIV infection.

There is clearly a true need for evidence-based, comprehensive sexuality education that meets the needs of all youth, including HIV positive, lesbian, gay, bisexual, and transgender youth. Congress should fund age-appropriate, comprehensive, and evidenced based sexuality education programs which fully inform youth about HIV prevention-interventions. Abstinence is and should remain a critical component of comprehensive HIV prevention education along with contraception and other life and decision making skills.

AIDS Action urges the Committee to provide the necessary oversight to bring an end to federal funding for abstinence-only-until-marriage programs. We ask Congress to act in the best interest of young people by supporting public health and education policies that are comprehensive and rooted in the best science. Thank you, Chairman Waxman for your leadership and commitment on this issue.

(DHHS) spoke before the committee in defense of abstinence-only programs.

"HHS' abstinence education programs are part of a broader strategy to combat teen pregnancy and STDs," Keckler testified. "Over the last five years, the department estimates that it has expended billions of dollars towards this effort."

While recent studies have not shown that abstinence-only programs are successful in reducing pregnancy and STDs, they also have not shown that the programs worsen these outcomes, Keckler noted.

"The administration believes that the abstinence education program sends the healthiest message as it is the only certain way to avoid out-of-wedlock pregnancy, and sexually transmitted diseases," Keckler said. "The great majority of American parents agree: a 2007 poll conducted by the National Campaign to Prevent Teen Pregnancy found that 90% of teens aged 12-19 and 93% of adults agree that it is important for teens to be given a strong message that they should not have sex until they are at least out of high school."

Waxman noted that U.S. taxpayers are showering funds on abstinence-only programs that don't work and ignoring comprehensive sex education programs that can delay sex and protect teens from disease and result in fewer pregnancies.

"We've already spent \$1.3 billion on abstinence-only programs," Waxman concluded. "The question we must ask today is whether we can justify pouring millions more into these programs when the weight of the evidence points elsewhere."

References

1. Underhill K, Operario D, Montgomery P. Abstinence-only programs for HIV infection prevention in high-income countries. *Cochrane Database Syst Rev.* 2007;(4):CD005421.
2. Trenholm C, Devaney B, Fortson K, et al. Impacts of abstinence education on teen sexual activity, risk of pregnancy, and risk of sexually transmitted diseases. *Jrl Policy Analysis Mang.* 2008;27(2):255-76.
3. Bruckner H, Bearman P. After the promise: the STD consequences of adolescent virginity pledges. *J Adolesc Health.* 2005;36:271-278. ■

'Good bacteria' may aid in slowing HIV spread

By Rebecca Bowers

This article originally appeared in the May

2008 issue of *Contraceptive Technology Update*

Early research indicates that beneficial bacteria found in the healthy vagina aids in reducing the amount of vaginal HIV among HIV-infected women and may make it more difficult for the virus to spread.¹

What's next in terms of research when it comes to determining the impact of the beneficial *Lacto-bacillus* bacteria in affecting HIV transmission? A logical next step would be to better understand factors that determine whether women, HIV-infected and HIV-negative, are colonized with *Lactobacillus*, particularly the species that produces hydrogen peroxide and other protective factors, says **Jane Hitti**, MD, associate professor in the Department of Obstetrics & Gynecology at the University of Washington School of Medicine in Seattle. Hitti, who presented study findings at the February 2008 Conference on Retroviruses and Opportunistic Infections, is part of a team of physicians and scientists at the University of Washington and the University of Rochester Medical Center who are working to learn more about how HIV survives and spreads.

"We should explore whether it is possible to establish *Lactobacillus* colonization among HIV-infected women who do not have this helpful bacteria, and if so, whether colonization alters vaginal HIV viral load," says Hitti.

What factors are needed to promote healthy vaginal flora? A healthy vagina is highly acidic, with a pH less than 4.7. This acid environment is achieved primarily by lactic acid, which is produced by human lactobacilli. With a low pH, the growth of acidophilic organisms such as lactobacilli are encouraged, and the growth of other organisms are inhibited. An elevated vaginal pH is associated with loss of hydrogen peroxide-producing lactobacilli, presence of bacterial vaginosis and trichomoniasis, acquisition of gonorrhea, and enhanced transmission of HIV.²

To conduct the current study, researchers followed a group of 57 HIV-infected women from Seattle and Rochester for up to five years. They looked at changes in their vaginal bacteria, as well as changes in the vaginal viral load and the plasma viral load.

The team found that women with hydrogen peroxide-producing *Lactobacillus* in the vagina had lower levels of HIV virus in their genital secretions. Findings also indicate that the amount of the HIV virus in the vagina varied in step with

the presence of *Lactobacillus*. Women who did not have the bacteria at first, but who had acquired it by a subsequent visit, had decreased vaginal HIV levels while vaginal HIV levels increased in women in whom the good bacteria had disappeared between visits.

Promote vaginal health

While previous work in the laboratory has indicated that *Lactobacillus* might help prevent HIV infection in women, the current study provides a direct link to decreased levels of the virus in the vagina with the presence of *Lactobacillus* that produce hydrogen peroxide there.

Jeanne Marrazzo, MD, MPH, associate professor in the Division of Allergy & Infectious Diseases at the Department of Medicine at the University of Washington, says, "I think the data to support that lactobacilli have a strong protective role in reducing women's risk of getting HIV and other sexually transmitted diseases [STDs] are really quite strong. However, we haven't yet figured out how to give women back their vaginal lactobacilli."

Promoting vaginal health is important for HIV-negative and HIV-infected women, she says. "We know that avoiding douching is important to keeping the lactobacilli healthy, but we don't yet have probiotics available to really recolonize vaginal lactobacilli," states Marrazzo.

Douching is not recommended for the prevention or treatment of vaginitis, according to the American College of Obstetricians and Gynecologists.³ In a study of 1,200 U.S. women at high risk for sexually transmitted infections, douching for symptoms or hygiene, particularly frequent or recent douching, was associated with bacterial vaginosis (BV) and bacterial vaginosis-associated vaginal microflora.⁴

What roles may probiotics play in vaginal health? While early research surrounding the effectiveness of the administration of lactobacilli for the treatment of BV are mostly positive, it cannot yet be concluded definitively that probiotics are useful for this purpose.⁵ Attempts are under way to formulate a *Lactobacillus* preparation that does not alter commensal bacteria²

References

1. Hitti J, Paul K, Agnew K, et al. Protective effect of vaginal *Lactobacillus* on genital HIV-1 RNA concentrations: Longitudinal data from a U.S. cohort study. Presented at the 15th Conference on Retroviruses and Opportunistic

Infections. Boston; February 2008.

2. Marrazzo JM. "Normal vaginal flora." In: A Practical Update on Sexually Transmitted Infections: Advances in Diagnosis and Treatment Highlights From a Symposium. Accessed at www.familypracticenews.com.

3. American College of Obstetricians and Gynecologists. Vaginitis. Washington, DC: 2006.

4. Ness RB, Hillier SL, Richter HE, et al. Douching in relation to bacterial vaginosis, lactobacilli, and facultative bacteria in the vagina. *Obstet Gynecol* 2002; 100:765-772.

5. Falagas ME, Betsi GI, Athanasiou S. Probiotics for the treatment of women with bacterial vaginosis. *Clin Microbiol Infect* 2007; 13:657-664. ■

One STEP forward, two steps back

The quest for an HIV vaccine goes on

The past year was a disappointing one in the search for a safe and effective HIV vaccine, said **Anthony S. Fauci**, MD, director, National Institute of Allergy and Infectious Diseases National Institutes of Health (NIAID).

"The scientific concept tested in the HIV vaccine study known as the STEP trial was considered to have great promise; however, the vaccine did not have the desired beneficial effect," he said. "Although the finding was disappointing, it was not unusual given the nature of science and vaccine development. Historically, it has taken decades to find effective vaccines to combat infectious diseases."

For example, it took 89 years to create an effective pertussis vaccine and 42 years to develop an effective measles vaccine, and then only after researchers experienced numerous setbacks and disappointments. "Yet they persevered," he said. "Finding a safe and effective HIV vaccine demands an equally intense resolve." The veteran AIDS fighter made the comments as the 25th anniversary of the discovery of virus was noted in May as part of HIV Vaccine Awareness Day.

"Since then, over 60 million people have been infected with HIV—an estimated 2.5 million in 2007 alone—numbers that remind us that the development of an HIV vaccine is an urgent humanitarian imperative," Fauci said.

Last year, 2.1 million people died as a result of AIDS, including 330,000 children under the age of 15. Today, 33.3 million people are living with HIV infection. Although the problem is most severe in sub-Saharan Africa, the United States also has been

hard-hit: more than 565,000 people in this country have died of AIDS and an estimated 1.1 million are living with HIV infection. African-Americans and Hispanics shoulder the greatest burden, accounting for 59 % of U.S. AIDS cases in 2006.

"In some urban areas, the HIV infection rates rival those of Africa," he said. "Nowhere is this more shocking than in the nation's capital, where one in 20 Washingtonians have HIV and one in 50 has AIDS."

Though much has been gained in the form of life-saving treatments, the stark reality is that for every person with HIV who is placed on therapy, about three more individuals become newly infected with the virus, he noted. "The rate of new HIV infections far outpaces our ability to supply a lifetime regimen of HIV medication to everyone who needs it," he said. "Further scale-up of lifesaving HIV treatment programs is critical. However, treatment alone will not end the AIDS pandemic."

Thus developing HIV prevention strategies, including a vaccine, remains an extremely important goal. A number of proven strategies to prevent HIV transmission are already available, including education and behavior modification; condom usage; medically supervised adult male circumcision; harm-reduction approaches such as needle and syringe exchanges for injection drug users; and antiretroviral drug regimens for HIV-infected pregnant women to prevent mother-to-child HIV transmission of the virus. NIAID is testing other prevention strategies, such as microbicide gels or creams that can be applied prior to sexual intercourse and preventive regimens of antiretroviral drugs, that we hope will prove successful. Ideally, a vaccine that prevents HIV infection would be a core component of our prevention program.

Recently, NIAID convened a scientific summit to examine the state of HIV vaccine research and determine how best to move the field forward. Based on that discussion, it became clear that although it is important to maintain our approach to identifying promising HIV vaccine candidates and clinically testing those candidates when appropriate, it also is imperative that we place greater emphasis on the basic research necessary to address the many unanswered questions that remain about HIV, Fauci noted. "We must understand how to create a vaccine that induces a protective immune response in people that is more effective than the immune response that results when someone is naturally infected with HIV," he said. ■



ABSTRACT & COMMENTARY

Gut punch: Persistence of HIV despite suppression

By **Dean L. Winslow, MD, FACP, FIDSA**, Chief, Division of AIDS Medicine, Santa Clara Valley Medical Center; Clinical Professor, Stanford University School of Medicine. Dr. Winslow serves as a consultant for Siemens Diagnostics, and is on the speaker's bureau for Boehringer-Ingelheim and GSK.

Summary: CD4+ T-cell depletion occurs in gut-associated lymphoid tissue (GALT) despite long term suppression of viremia by HAART. Higher levels of proviral DNA exist in GALT than in peripheral blood lymphocytes (PBMCs) of aviremic patients. Cross-infection between these two compartments appears to occur.

Source: Chun T-W, et al. Persistence of HIV in gut-associated lymphoid tissue despite long-term antiretroviral therapy. *J Infect Dis.* 2008;197:714-720.

Eight hiv-infected patients (mean CD4+ t cell count 622 cells/uL) who had been receiving effective HAART for an average of 8.4 years were included in this study. PBMCs were obtained by leukapheresis and endoscopic terminal ileum biopsies were performed to obtain samples of Gut-Associated Lymphoid Tissue (GALT). Standard techniques, including fluorescence-activated cell sorting (FACS), were used to separate various subpopulations of lymphocytes. Quantitative real-time PCR was used to measure HIV DNA.

While the percent age of CD4+ T cells in GALT was slightly lower than that in peripheral blood in HIV-negative individuals (40% vs 65%), the mean %age of CD4+ T cells in these eight study participants was only 11.3%, suggesting incomplete recovery of CD4+ T cells in this compartment despite years of effective viral suppression in these patients.

FACS-enriched resting (CD25-/CD69-/HLA-DR-) and activated (CD25+/CD69+/HLA-DR+) CD4+ T cells in blood and CD8-depleted cells obtained from GALT were subjected to quantita-

tive PCR for detection of HIV DNA. The frequency of cells carrying proviral DNA was highest in GALT (mean 4887 cells per million CD4+ T cells) vs resting T cells (mean 1083 cells per million CD4+ T cells) and activated T cells (mean 1796 cells per million CD4+ T cells).

Phylogenetic analysis of HIV env sequences from GALT and the two peripheral blood compartments showed a high degree of relatedness, suggesting trafficking/cross-infection between the three compartments.

Commentary

I remember vividly a comment made by Hans Wigzell (Karolinska Institute) in a lecture he gave at the DuPont Company around 1986, "Remember — the final battle of HIV infection is fought in the lymph nodes!" GALT is the largest component of the human lymphoid system.

This important study from Tony Fauci's own Laboratory of Immunoregulation at NIAID highlights the excellent work for which this group has been known over the years. This carefully-performed study provides insight into the pathogenesis of HIV infection and conclusively confirms findings from small earlier studies in which profound CD4+ T cell depletion in GALT in HIV-infected patients was observed despite effective antiretroviral therapy.¹ Similar degrees of CD4+ T cell depletion have been seen with SIV infection in macaques.² Due to the relatively free trafficking of lymphocytes between the peripheral blood and GALT compartments, this GALT CD4+ lymphopenia has implications for systemic immunodeficiency, as well as local immunodeficiency, nonspecific gastrointestinal symptoms, and opportunistic infections commonly seen in HIV infection. The surprisingly high levels of proviral DNA in GALT, despite relative gastrointestinal CD4+ lymphopenia in these aviremic patients, likely also provide an explanation for some of the viral dynamics of long-term persistence of low-level viremia in patients on antiretroviral therapy (as demonstrated in the previously reviewed paper by Sarah Palmer).³

[This article originally appeared in the May 2008 issue of Infectious Disease Alert.]

References

1. Guadalupe M, et al. Severe CD4+ T-cell depletion in gut lymphoid tissue during primary human immunodeficiency virus type 1 infection and substantial delay in

restoration following highly active antiretroviral therapy. *J Virol.* 2003;77:11708-11717.

2. Veazey RS, et al. Gastrointestinal tract as a major site of CD4+ T cell depletion and viral replication in SIV infection. *Science.* 1998;280:427-431.

3. Palmer S, et al. Low-level viremia persists for at least 7 years in patients on suppressive antiretroviral therapy. *PNAS.* 2008;105:3879-3884. ■

CDC: Number living with HIV on steady rise

New cases stable, survivors increasing

From 2003 through 2006, the estimated number of HIV/AIDS cases in the 33 states with confidential name-based HIV infection reporting remained stable, with 18.5 cases per 100,000 population, the Centers for Disease Control recently reported.¹ Though the total number of new cases of HIV/AIDS remained stable in the 33 states, HIV/AIDS prevalence (i.e., the number of persons living with HIV/AIDS) increased steadily: By the end of 2006, an estimated 491,727 persons in the 33 states were living with HIV/AIDS.

The CDC report presents estimated numbers of cases of HIV/AIDS (cases of HIV infection, regardless whether they have progressed to AIDS) from the 38 areas (33 states and 5 U.S. dependent areas) that have had confidential name-based HIV infection reporting for a sufficient length of time (i.e., since at least 2003) to allow for stabilization of data collection and for adjustment of the data in order to monitor trends. According to the number of reported AIDS cases, these 33 states represent approximately 63% of the epidemic in the 50 states and the District of Columbia. The 2008 surveillance report includes the following the trends and highlights:

Age group: From 2003 through 2006, the estimated number of newly diagnosed HIV/AIDS cases decreased among children (less than 13 years of age) and in the following age groups: 13-14, 30-34, and 35-39 years. The estimated number of HIV/AIDS cases remained stable among persons aged 40-44 years and increased among persons aged 15-19, 20-24, 25-29, 45-49, 50-54, 55-59, 60-64, and 65 years and older. In 2006, the largest number of HIV/AIDS cases occurred among persons aged 40-44 years, who accounted for 16% of all HIV/AIDS cases diagnosed during that year.

Race/ethnicity: From 2003 through 2006, the estimated number of newly diagnosed HIV/AIDS

cases increased among whites and Asians/Pacific Islanders, remained stable among blacks and Hispanics, and fluctuated among American Indians/Alaska Natives. Blacks accounted for 49% of all HIV/AIDS cases diagnosed in 2006. In 2006, rates of HIV/AIDS cases were 67.7 per 100,000 in the black population, 25.5 per 100,000 in the Hispanic population, 8.8 per 100,000 in the American Indian/Alaska Native population, 8.2 per 100,000 in the white population, and 6.7 per 100,000 in the Asian/Pacific Islander population.

Sex: From 2003 through 2006, the estimated number of HIV/AIDS cases increased approximately 5% among males and decreased 6% among females. In 2006, males accounted for 74% of all HIV/AIDS cases among adults and adolescents. In 2006, rates were 33.8 per 100,000 among males and 11.5 per 100,000 among females.

Transmission category: From 2003 through 2006, the estimated number of HIV/AIDS cases increased among men who have sex with men (MSM) and remained stable among adults and adolescents with HIV infection attributed to high-risk heterosexual contact (heterosexual contact with a person known to have, or to be at high risk for, HIV infection). The estimated number of HIV/AIDS cases decreased among injection drug users (IDUs), MSM who were also IDUs, and among children. MSM (49%) and persons exposed through high-risk heterosexual contact (33%) accounted for 82% of all HIV/AIDS cases diagnosed in 2006. Of all HIV infections diagnosed in 2005 in the 33 states with confidential name-based HIV reporting, 38% progressed to AIDS within 12 months after HIV infection was diagnosed. AIDS was diagnosed within 12 months after the diagnosis of HIV infection for larger proportions of persons aged 13-14 years and 35 years and older, for Hispanics, for IDUs, and for males with HIV infection attributed to high-risk heterosexual contact.

Persons living with HIV/AIDS

From 2003 through 2006, the estimated number of persons living with HIV/AIDS increased

CE/CME questions

16. Which of the following statements about HIV infection and heart disease is true?
 - A. HIV patients who are treated with protease inhibitors are at a greater risk of heart disease than are HIV patients who are not treated with PIs, but who smoke and are obese
 - B. HIV patients who smoke, are obese, and who have high blood pressure and high cholesterol are a greater risk of heart disease because of these lifestyle and health issues than they are from their use of protease inhibitors
 - C. Non-protease inhibitor therapy poses a greater heart disease risk to HIV patients than do PI drugs
 - D. None of the above

17. HIV patients who have six or more life stressors are at considerable more risk of what than patients who have zero or one life stress, according to a recent study?
 - A. Not adhering to their antiretroviral therapy
 - B. Committing suicide
 - C. Heart disease
 - D. All of the above

18. At a recent Congressional hearing, scientists and other experts reported which findings about the success of abstinence-only education programs?
 - A. Abstinence-only programs result in a greater percentage of students delaying sex and avoiding STDs and pregnancy over a 2 year period
 - B. Abstinence-only programs result in fewer HIV infections over a 10 year period
 - C. Abstinence-only programs when compared to control groups demonstrate no difference in pregnancy rates, sexual initiation age, pregnancy rates, and sexually-transmitted disease rates
 - D. None of the above

Answers: 16. (b); 17. (a); 18. (c)

COMING IN FUTURE MONTHS

■ Potential new drug in CCR5 antagonist class enters Phase III trials

■ Study refines adherence measurements

■ Here's the latest research from the International AIDS conference

■ Increased focus on testing opens doors to more new HIV patients

steadily in the 33 states. At the end of 2006, an estimated 491,727 persons in these states were living with HIV/AIDS. By age group, most (21%) were aged 40-44 years. By race/ethnicity, 47% were black, 34% white, 17% Hispanic, and less than 1% each were American Indian/Alaska Native or Asian/Pacific Islander. By sex, 73% of adults and adolescents living with HIV/AIDS were male.

Of the estimated 353,825 male adults and adolescents living with HIV/AIDS, 62% had been exposed through male-to-male sexual contact, 17% had been exposed through injection drug use, 13% had been exposed through high-risk heterosexual contact, and 7% had been exposed through both male-to-male sexual contact and injection drug use. Of the estimated 131,195 female adults and adolescents living with HIV/AIDS, 73% had been exposed through high-risk heterosexual contact, and 26% had been exposed through injection drug use. Of the estimated 6,703 children living with HIV/AIDS, 92% had been exposed perinatally.

Reference

1. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2006. Vol. 18. Atlanta: U.S Department of Health and Human Services, Centers for Disease Control and Prevention; 2008: at <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>. ■

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CNE/CME objectives

The CNE/CME objectives for *AIDS Alert*, are to help physicians and nurses be able to:

- Identify the particular clinical, legal, or scientific issues related to AIDS patient care;
- Describe how those issues affect nurses, physicians, hospitals, and clinics;
- Cite practical solutions to the problems associated with those issues.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any question answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.